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SURGERY IN METABOLIC DISEASES

Collective Review

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FIFTY years ago our knowledge of diseases of the metabolism was very limited and vague. As in other fields of medicine, increased clinical experience and extensive investigative work have enabled us to acquire a more intelligent understanding of this group of diseases. It was only twenty years ago that we began to master the fear of operating upon certain glands of internal secretion, but since then many notable advances have been made in the surgery of metabolic diseases. Obstacles have been overcome which heretofore had made surgical treatment of these syndromes either extremely hazardous or impossible. It would be too lengthy to consider adequately all the metabolic diseases which have been either cured or controlled to some extent by surgical treatment. In this review, surgery of the thyroid, the surgical diabetes, hyperinsulinism, hyperparathyroidism, and tumors of the adrenal glands with metabolic changes will be considered. Lesions of the ovaries and pituitary gland which commonly produce metabolic changes will only be touched upon as is necessary for a complete discussion of the chosen topics. Collectively, the subjects under consideration are exemplary as to the progress made and to be made in the field of surgery.

THYROID DISEASE

Diseases pertaining to the thyroid gland are the most frequent metabolic disturbances which require surgical treatment. The patients were very fearful of operations performed upon the thyroid gland in the early days, and rightfully so, because of the high operative mortality. However, in the last few decades, numerous contributions have been made to the preoperative, operative, and postoperative management of these cases. Consequently the operative results have improved, and the mortality of thyroidectomy has been greatly reduced. In some large goiter centers, the mortality for thyroidectomy is 1 per cent or less. The preoperative management of the patient suffering from a toxic goiter has been more or less standardized, and today the patient is so prepared that thyroidectomy is performed at the most favorable time for each individual case.

Iodine was known to be of beneficial value in hyperthyroidism for many centuries; however, the work of Plummer (67) in 1923 in instituting its preoperative use on a rational basis is perhaps the most important advance in the preoperative preparation of this group of cases. We now know the dangers of prolonged and indiscriminate use of this drug, and have learned to recognize the so-called iodine-fast, as well as the "burned out" thyroid patient. Today most medical centers have developed a routine for the management of both of these types of patients. That the thyroid gland plays a principal role in the metabolism of iodine in the body is not surprising when we realize that a gland which weighs only 20 gm. contains one-fifth of all the iodine in the body. Salter (71) found that not more than 10 per cent of the iodine in the thyroid gland was inorganic in nature; 90 per cent or more was in organic combination and approximately two-thirds of this was in the form of di-iodotyrosine and one-third, tyrosine. In 1927 Harrington and Barger (41) showed that thyroxine was a derivative of tyrosine. Hinton (45) believes that failure to supply an adequate amount of tyrosine to the thyroid gland because of a disturbance in the protein

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metabolism may be a potent factor in the production of thyroid disease. The first comprehensive work published on the determination and significance of blood iodine was that by Kernan and Lahey (66). Since then it has been repeatedly demonstrated that the blood iodine is elevated in hyperthyroidism, and returns to normal following thyroidectomy. The preoperative estimation of blood iodine has assisted in establishing the diagnosis and evaluating the severity of this disease. In 1939 Perkin and Cattell (65) reported preoperative and postoperative blood iodine levels on 256 cases of exophthalmic goiter, and analyzed the relation of these levels to the recurrence of hyperthyroidism. One hundred of these patients were followed up for one year. It was noted that the number of patients who showed a normal blood iodine level after subtotal thyroidectomy decreased with the duration of symptoms before treatment. The majority of patients with symptoms for one year had a normal blood iodine level, and following subtotal thyroidectomy, the level was increased. The incidence of recurrence in these patients was 19.7 per cent. If symptoms of hyperthyroidism were present from four to five years, the blood iodine level was generally normal and usually uninfluenced by subtotal thyroidectomy. It was believed that these findings could be used as an index of the amount of thyroid gland to be removed in patients with thyrotoxicosis.

In 1942 Hinton (45) reported a study on blood iodine in 235 patients who had, or were suspected of having, thyroid disease. In 34 patients the hyperthyroidism was of more than one year's duration, but in these cases, he found the blood iodine was elevated, which was in contrast to the findings of Perkin and Cattell (65). In 16 patients with persistent or recurring hyperthyroidism, the incidence of an elevated blood iodine was no greater than that observed in nonthyroid patients. This strongly suggests an error in the diagnosis of hyperthyroidism, and that the decreased iodine content of the blood is not indicative of exhaustion of the thyroid gland. Many clinicians believe that blood-iodine levels will supplant the basal-metabolism estimations in the future, when a simpler method for their estimation is devised.

Another contribution of significance is the use of oxygen in thyroid crises. The clinical appearance and well-being of the patient responds promptly to oxygen therapy. We have learned through the use of oxygen, that anoxia is a significant factor in the tachycardia of thyrotoxicosis. This is best illustrated by the patient who leaves the operating table with a pulse rate of approximately 100, but because of the diminished oxygen obtained from the atmosphere as compared with that obtained from the anesthetic mixture, his pulse promptly rises to 130 or more. For the past ten years I have had oxygen administered to all patients whose pulse rate was above 120 upon their return from the operating room. In some cases the tachycardia responds in a few hours; however, since the adoption of this routine, the postoperative course of the very toxic cases has been much smoother.

In 1930 Lahey (52) brought to our attention a type of hyperthyroidism which he called apathetic hyperthyroidism. He stated that this condition remained undiagnosed for long periods, and when diagnosed the degree of toxicity was underestimated. In an analysis of his cases, he noted that his mortality was largely related to the apathetic type of hyperthyroidism. This type is seen in the later decades of life, and the clinical and physical findings would not impress one as being those of severe hyperthyroidism. They present a picture simulating a mild form of the disease with a slight loss of weight over a period of several years: the skin is dry and wrinkled, and instead of the characteristic stare and marked nervousness of severe hyperthyroidism, they present an apathetic face, and the basal metabolic rate is only slightly elevated. At the operating table, the patients apparently withstand the operation very well; in most instances the pulse rate remains well below 100 throughout the procedure. The postoperative course is very satisfactory for the first twenty-four to thirty-six hours; then drowsiness develops, which becomes progressively worse, and finally the patient goes into coma and dies very peacefully. This is quite a different picture from that customarily seen when a toxic thyroid patient succumbs in a thyroid crisis following thyroidectomy. Lahey pointed out that these patients are more seriously ill than we formerly realized. He recommended that after careful preoperative preparation, thyroidectomy should be performed as a two-stage procedure with approximately six weeks between stages. By this method of treatment, the mortality in this group was practically eradicated. This contribution has sharpened our diagnostic acumen, and we now know that this type of thyrotoxicosis is much more prevalent than we formerly believed. Lahey not only brought to our attention the fact that this type of hyperthyroidism is frequently missed entirely by the clinician, but also pointed out that many patients die from this condition following an operation for a pathological lesion elsewhere in the body. This further substantiates the dictum which we learned from experience, of the

proper time to treat the foci of infection in a patient suffering from this disease; namely, that in a patient suffering from hyperthyroidism, surgery other than that directed at the thyroid, though it may be minor in character, may precipitate a severe thyroid crisis, or be the cause of a fatality.

Considerable interest has been stimulated recently in the alterations in the calcium and phosphorus metabolism in hyperthyroidism. In 1891 von Recklinghausen (69) first described the demineralization of the skeleton in a case of hyperthyroidism of many years' duration. Subsequently Koeppen (51) and Askanazy (6) reported similar cases. In these early cases, the pronounced demineralization was apparent at autopsy when the bones were being studied. It was many years later before the picture of general osteoporosis was demonstrated clinically in a case of hyperthyroidism by the roentgenologists. In 1929 Plummer (68) and Dunlap and Moore (31) reported 5 cases of hyperthyroidism in which there was pronounced demineralization of the skeleton. In 2 cases the bone changes were so extensive that metastatic malignancy was considered. It is generally believed that the demineralization involves practically the entire skeleton. The small and flat bones usually show the change first, and later it is evident in the spine and long bones. Shrinking of the general stature, kyphosis, and flaring of the lower ribs have all been reported. A few cases of spontaneous fracture due to the demineralization are now appearing in the literature. In 1942, Bothe, Simpson and Rowntree (13) reported a case in which the patient, suffering from long-standing hyperthyroidism, had both spontaneous and traumatic fractures of the spine. Aub and his coworkers (7) reported an increase in the excretion of calcium and phosphorus in the feces and urine in clinical hyperthyroidism; therefore, just as in cases of hyperparathyroidism, we may have patients with hyperthyroidism in a negative calcium balance. This has been confirmed by other investigators.

In the last few years, many extensive studies have been made of the degree of liver damage and diminshed liver function in patients suffering from hyperthyroidism. Jaundice has frequently been observed in severe hyperthyroidism. Weller (81) and Beaver and Pemberton (9) found variable types of hepatic pathology in patients who succumbed to thyrotoxicosis. They observed acute changes consisting largely of degenerative fatty infiltration and a chronic lesion described by Weller as a patchy, chronic, parenchymatous interlobar hepatitis. Many investigators believe that further evidence of liver damage is the fact that the liver of a patient suffering from hyperthyroidism is unable to store glycogen in normal amounts. Numerous efforts have been made to determine whether these evidences of liver damage were of any significance or relation to the clinical picture of thyrotoxicosis, particularly the thyroid crises. Youmans and Warfield (84) were able to show impairment of liver function in 50 per cent of 44 patients with hyperthyroidism. Mills (62), using the galactose test, carefully studied a small group of patients and demonstrated a diminished liver function in the presence of hyperthyroidism, which disappeared following relief of the disease by thyroidectomy.

Others believe that the hippuric-acid test is more valuable than the galactose test, in that it gives us a reliable index of one clinically important hepatic function, namely, the function of detoxification. Chesky et al. (21) made a very careful study of the liver functions determined by the hippuric-acid test in more than 300 goiter patients admitted for surgery. Under the routine treatment which we all use for thyroid crises or severe hyperthyroidism, most patients showed improvement in liver function; in some the improvement was very slight; in others progressive hepatic insufficiency was observed. In view of these findings, the patients with the most severe liver damage received, in addition to the routine treatment, intravenous glucose with or without insulin, insulin by hypodermic injection, bile salts, liver concentrate, and glycine. In every case so treated, the liver function was either greatly improved or restored to normal. They also demonstrated decreased liver function after thyroidectomy. The decrease was most pronounced in the first forty-eight hours after operation; improvement followed thereafter. Chesky and his associates (21) did not contend that the hippuric-acid test should supplant clinical judgment as to operative risk, but suggested serial hippuric-acid tests in severe cases of hyperthyroidism as an aid in evaluating the response of the liver to this treatment. Some investigators believe that damaged liver function plays such an important part in thyroid crises that they should be called liver crises. This contention is gaining weight in that more cases have been reported in which the treatment of the liver damage has been very helpful in the severe crises.

The interrelationship between the thyroid and the anterior portion of the pituitary gland is far from being clearly understood. It has been shown that the thyroid-stimulating thyrotropic hormone elaborated by the anterior pituitary is an entity

separate and distinct from the other trophic principals which can be demonstrated in the extracts of fresh anterior-lobe substance such as the gonadotropic, adrenotropic, diabeticogenic, parathyrotropic, and mammotropic hormones. In 1929 Loeb and Basset (55) reported the production of hyperplasia of the thyroid gland in the guinea pig by the injection of extract of the anterior pituitary lobe. Later Collip (25) and Selye (73) showed experimentally that the pituitary and thyroid glands can be definitely enlarged in the female rat by the prolonged administration of hormone of the anterior pituitary lobe, and that the enlargement of both these organs ran approximately parallel to the weight increase in the ovaries. These findings suggest that there may be cases of hyperthyroidism that are pituitary in origin. Thompson and his associates (78) studied the effect of the administration of pituitary extracts containing the thyrotropic principle to 71 patients. In 39, or 56 per cent, there was an increase in the basal metabolic rate. In patients requiring more than one series of injections, it was of interest to note that the increases were greater in the first series of injections, and that the second course of treatment usually, but not invariably, failed to produce any increase in metabolism. Thompson concluded that the inincreased metabolic activity was temporary, in spite of prolonged treatment, and that the metabolism eventually returned to its level before treatment or even to a lower level. No increase was noted in 4 patients with marked myxedema, but in patients with mild or moderated hypothyroidism, the rate could be raised to normal; in patients with nontoxic goiter a thyrotoxic state could be produced temporarily; and in patients with exophthalmic goiter, the disease could be made temporarily more severe. It appeared that the effect could be produced only in patients with thyroid tissue capable of responding. If these observations were confirmed by others it would tend to discredit the thought that the pituitary gland may be the etiological factor in some cases of thyrotoxicosis.

Recently we have been able to differentiate more satisfactorily the types of chronic thyroiditis. In 1896 Riedel (70) described the type of thyroiditis which bears his name. In 1912 Hashimoto (43) described a second type in which there was a lymphocytic infiltration throughout the gland. In 1922 Ewing (33) stated that they were one and the same disease, and that the histological picture found in Hashimoto's disease was the early stage of Riedel's struma. This was very widely accepted until the work of Graham (39) in 1931 showed rather conclusively that they were two distinct pathological processes. An analysis of the reported cases showed that Riedel's struma, which was supposed to be the later stage of the disease, occurs earlier in life than does Hashimoto's disease. Riedel's struma occurs in both sexes and is unilateral in from 40 to 60 per cent of the reported cases, whereas Hashimoto's disease occurs only in the female, and is always bilateral. Myxedema is more common in Hashimoto's disease than in Riedel's struma. If the gross pathological appearance and the microscopical findings in a frozen section lead to the diagnosis of Hashimoto's disease, only half of the gland should be removed, in the hope that it will postpone or possibly prevent the development of this complication. In Hashimoto's disease the pathology is confined to the thyroid gland, whereas in Riedel's struma it frequently extends through the capsule into extrathyroid tissue. This explains the frequent occurrence of grave pressure effects in Riedel's struma, and the relative infrequency of severe pressure symptoms in Hashimoto's disease. The gland is firm in Hashimoto's disease but does not become stony hard as it usually does in Riedel's struma. Even though a clinical diagnosis of either type of thyroiditis seems apparent, the firm consistency of the gland makes it necessary to explore all such cases to exclude malignancy.

In the last few decades, there have been no outstanding changes in the operative technique of thyroidectomy which have aided in the reduced mortality. However, both the mortality and postoperative complications have been greatly decreased by the modern method of administering anesthetics by a well trained physician anesthetist.

There are several steps which, many surgeons believe, have improved the operative results; namely, the division of the thyroid gland at the isthmus, and the elevation of the lateral lobes before the resection is begun. Lahey (53) suggested the routine dissection and demonstration of the recurrent laryngeal nerve. He feels rather strongly that the strip of tissue which is left over the recurrent nerve, in the technique usually employed, results in leaving too much thyroid tissue, and may be the basis for the persistence or recurrence of the hyperthyroidism. In the hands of a master surgeon such as Lahey, this procedure offered no difficulty and has been free from complications; however, I believe it is safe to say that many surgeons performing thyroidectomies would rather not deliberately expose the nerve, lest they may injure it.

SURGICAL DIABETES

Since the discovery of insulin by Banting and Best in 1921, surgery performed upon the diabetic has become more and more specialized, and the fear of both the patient and the surgeon has been conquered in a large measure by the excellent operative results obtained. The management of the diabetes has become so intricate that fortunately very few surgeons attempt to treat this feature of the case. Unquestionably, the most important factor in obtaining the excellent results has been the combined management of the surgical diabetic by the metabolist and the surgeon throughout the preoperative, operative, and postoperative periods. There are very few communities which do not have this combined service available. This field is all the more important when we realize that the number of diabetics in the United States has increased tremendously in the past fifteen years. It is now estimated that from 1½ to 2 per cent of the population of the United States are either diabetics or potential diabetics. The increase in the number of diabetics is not distributed uniformly throughout life or in either sex, but has been shown to occur to a greater extent in children and in women between forty and sixty years of age. In both of these age groups operations are frequently required, not only for conditions commonly associated with diabetes, but for lesions entirely foreign to the disease. Many predict that the stress and strain of the present emergency will further increase the number of diabetics.

The diabetes adds little or nothing to the operative risk in operations of election. This is true only if the diabetes and the general metabolic state is adequately controlled preoperatively by the metabolist. Hence, under proper preparation the diabetic of today is as good an operative risk as the condition of his cardiovascular system indicates. In emergency cases, particularly those complicated by infection, the operative risk is greatly increased, and the closest co-operation between the medical and surgical departments in the management of these cases cannot be overemphasized.

Many diabetics are controlled more easily with protamine zinc insulin. Unfortunately, it has proved unsatisfactory to use insulin in this form in the surgical diabetic, as its action may become cumulative at any time. For this reason, we have discontinued the use of protamine zinc insulin during the immediate preoperative and postoperative periods and instead use either regular or crystalline insulin. The insulin requirements of the surgical diabetic may diminish very rapidly as the operation frequently relieves the condition which created the need for a greater insulin requirement. This is seen most frequently after adequate drainage of an infection or in the preoperative treatment of severe hyperthyroidism associated with diabetes. If this possibility is not anticipated, both the preoperative and postoperative periods may be complicated by severe insulin shock.

Frequently the abdominal pain in the diabetic is difficult to evaluate. The earlier symptoms and physical findings of acidosis, which may closely simulate those found in acute abdominal conditions, have been clearly demonstrated. Even leucocytosis and fever, so characteristic of the acute abdominal condition, are associated with acidosis in a high percentage of cases. We no longer wait until the patient is drowsy or about to go into coma before acidosis is considered. These clinical findings are neurological manifestations of the terminal stages of acidosis.

When this clinical picture occurs, the surgeon is often called upon to differentiate between acidosis and a surgical condition of the abdomen; frequently it is only the urine examination and the blood-sugar and carbon-dioxide determinations which enable him to arrive at the proper diagnosis. If acidosis is present it should be controlled before surgery is performed. As a rule, this takes only a few hours and there are very few emergencies in which the risk of operation is increased as much by this delay as by performance of the operation in the presence of acidosis. If the emergency will permit, operation should be postponed until the carbon dioxide is 50 volumes per cent; in extreme cases an operation may be done with a carbon dioxide of 40 volumes per cent. Regardless of the findings upon examination of the abdomen when acidosis is found, as soon as this complication is controlled, another careful abdominal examination should be made to rule out a coexisting lesion which may require surgical treatment.

In conjunction with Beardwood (12), a study was made to evaluate the abdominal symptoms of the diabetic in comparison with those of the nondiabetic. It was found that the most severe abdominal pain occurs in a diabetic acidosis; in the absence of acidosis, other things being equal, the abdominal pain due to an underlying pathological process is less severe in the diabetic than in the nondiabetic. The last portion of the findings has proved most valuable since there was a tendency to underestimate the presence of a surgical lesion in the abdomen of a diabetic, as the symptoms and physical findings did not appear

to be severe enough. In a series of more than 50 diabetics who had lesions in the abdomen associated with pus, acidosis did not occur in a single case. This is contrary to our experience with diabetic patients who had small collections of pus elsewhere in the body.

Even though acidosis is the most hazardous complication in the surgical diabetic, infection is the most common and a serious one. The diabetic has a lowered local and general resistance to infection on account of the cardiovascular disturbance (primarily arteriosclerosis) and the abnormal carbohydrate metabolism. If localization of the infection is not apparent and lymphatic involvement occurs, the surgical risk is great. Sepsis is borne very poorly by the diabetic, and treatment should be directed toward the infection rather than the diabetes. A vigorous attempt to make the patient's urine sugar-free is to be avoided. It is better to drain or remove the infectious process, as then the carbohydrate metabolism will improve. The blood-sugar level need not influence the decision to operate, provided that the carbon dioxide is in the region of safety. In some cases of gangrene it has been necessary to incise and drain a collection of pus to control the diabetes, even though the carbon dioxide was a little lower than desired.

In the past we applied antiseptics locally in a very weak form in the diabetic, but this handicap has been overcome with the discovery of the sulfonamides. The 10 per cent sulfathiazole ointment has been used with excellent results in patients with diabetic gangrene involving only the digits. The number of patients successfully treated by conservative surgery has been increased by the use of this therapeutic agent. In more extensive processes the local application of microcrystals of sulfathiazole in conjunction with the oral administration of this substance has universally proved to be the most effectual treatment. In spite of these favorable reports, experience shows that we should not procrastinate in the employment of radical surgery when it is indicated by the local findings and not contraindicated by the patient's general condition. Zinc peroxide when applied as suggested by Meleney and Johnson (61) has proved very beneficial in chronic infectious processes complicated by sinus formation.

Gangrene is perhaps the most common as well as one of the most serious infectious processes which we encounter in the diabetic. There is a wide variation in the mortality rate in the various series of cases of diabetic gangrene as reported by well organized services for diseases of the metabolism. An analysis of the figures shows that the mortality is in direct proportion to the percentage of cases complicated by extensive and severe infection, and that the highest mortality occurred among the diabetics admitted to the hospital in a very toxic state, who usually have a gangrenous process which will not localize. In this last group refrigeration of the involved part, as advocated by Allen (4), bids fair to become a therapeutic measure which will enable us to treat the condition with much greater success and greatly reduce the mortality. In his early reports Allen emphasized the fact that metabolic activity is lowered when the temperature of the tissues has been reduced, and he suggested that we lower the temperature of the infected parts in patients having a peripheral vascular lesion from which very toxic substances are absorbed. In his experimental work on animals, he applied a tourniquet at the site elected for amputation and kept the extremity distal to the tourniquet at 5° C. After the leg was kept at this temperature for several hours, he demonstrated that amputation could be done at the level at which the tourniquet was applied, or the upper limit of refrigeration of the tissues, without anesthesia. Thus, he has not only demonstrated a means of diminishing the toxic state of the patient, which permits surgical intervention with a much greater degree of safety, but he has also shown that amputation can be performed through the refrigerated tissue without the use of an anesthetic. Recently Allen (4) reported 45 cases of gangrene in which the local application of refrigeration had been used; the results were most gratifying.

There are three distinct divisions (Table I) in the use of refrigeration in surgery (3); (1) its use preceding operation with a tourniquet; (2) its postoperative application to the flaps; and (3) its prolonged use without a tourniquet, for preoperative preparation in certain cases, or when an uncertainty exists as to whether operation is necessary.

When tissue is refrigerated in preparation for operation, it is important to realize that the tissues are not frozen, but are kept between 5° and 10° C., and as near 5° C. as possible. Necrosis or frostbite do not occur. This procedure is based on the fact that tissues have been kept alive for long periods in an ice box. When properly applied, refrigeration will produce surgical anesthesia. The fundamental principle of refrigeration for surgical anesthesia is that cold nerves cannot transmit impulses and cold tissues cannot respond with shock or any other harmful reaction. Superficial chilling of the skin may produce enough anesthesia

for a superficial operation; i.e., skin grafting. For a deeper operation a tourniquet is indispensable. The length of time required for preparatory refrigeration is still not definite. Allen found that with thin, weak patients with arteriosclerosis, the most plausible time is as follows: for a thigh amputation, two and one-half hours; for disarticulation at the knee or through the middle of the leg, two hours; for the lower half of the leg or the foot, one and one-half hours; and for the metatarsus or the toes, one hour. If the tourniquet is properly applied and securely fastened and the chilling is continuous to all parts at the correct temperature, there is complete local anesthesia so that the patient is not aware when the nerve is cut or the bone is sawed. It is still not certain whether the tourniquet should be placed at the site of amputation and the refrigeration carried on several inches or a number of inches above the level of amputation.

Ice is applied to the flaps after the operation, and the lower temperature produced reduces the local metabolism so that a limited blood supply may be adequate for the need, and this diminishes the tendency to sloughing. It also aids by inhibiting pain, edema, and bacterial activity. The principle of refrigeration need not be confined to peripheral vascular lesions; it has been used in crushing wounds of various types. Arteriosclerotic legs have been packed in ice for periods up to one month without a tourniquet until the patient gained sufficient strength for an ultimate successful amputation. Prolonged refrigeration without a tourniquet has been used in extensive gangrene, with the result that advancing gangrene, infection, and systemic intoxication have been checked. It has been shown that gangrene of both arteriosclerosis and embolism can be delayed by reduced temperature.

Quite extensive studies have been made of the vascular tree of the legs which have been amputated for diabetic gangrene. This was done by Henderson and Beardwood (44) by means of a mercurial injection of the arterial tree at what was the patient's mean pressure. As a control, the blood vessels of normal amputated legs, both of children and adults, were included in the study. The specimens were then x-rayed to obtain a picture of the vascular tree. Among other things it was clearly demonstrated that if a patient has had diabetes a long time before gangrene occurs, a rich collateral circulation develops, whereas if a patient has only had diabetes for a short period of time before the gangrene occurs, there is very little evidence of a collateral circulation. This finding has enabled us to be more conservative in the management of a gangrenous process of the digits in a known diabetic of many years' standing. On the other hand, the lack of a developed collateral circulation is in keeping with the poor response to local measures of a gangrenous process of the digits in a patient who has had diabetes only for a short time. In the last ten years there has been an increasing number of cases in which successful conservative surgical procedures have been performed when the diabetes had been present for a number of years, and it is believed that the explanation can be found in these studies.

TABLE I.—THREE DIVISIONS IN THE USE OF REFRIGERATION

1. Preceding operation with tourniquet (for anesthesia)
   a. For thigh amputation 2½ hrs.
   b. Disarticulation at knee 2 hrs.
   c. Amputation at middle of leg 2 hrs.
2. Postoperative application (applied to flaps)
   a. Lowers metabolism, less blood supply necessary to nourish tissue and less sloughing
   b. Inhibits pain, edema, and bacterial activity
3. Prolonged use without tourniquet
   a. Arteriosclerotic legs in ice
   b. In extensive gangrene to check infection and toxic absorption.

The newer physiological concepts of diabetes have pointed to the fact that many endocrine glands other than the pancreas may play an important role in its syndrome. While surgical attempts to help or cure this disease to date have proved unsatisfactory, when the physiological pathology of diabetes is completely understood it is not beyond the realm of hope that the surgeon may be able to relieve this metabolic disorder.

HYPERINSULINISM

In 1924 Harris (42) described an entity which he believed was due to an excessive secretion of insulin, and was characterized by periods of hypoglycemia. He called it hyperinsulinism, and reported his several cases in minute detail. Since his excellent contribution, considerable investigative work has been done upon the hypoglycemic state which occurs in hyperinsulinism. In 1927, Wilder and coworkers (83) reported a case of hyperinsulinism which was operated upon by W. J. Mayo. At operation he found a carcinoma of the islands of Langerhans with metastasis to the liver. Extensive studies were carried out upon this case, including the evaluation of the amount of insulin in the tumor. In metastatic nodules from the liver, they were able to isolate as much as 40 units of insulin from 100 gm. of the tumor. In 1929, Howland, Campbell, Maltby and Robinson (48) reported a case in which Roscoe Graham successfully removed a benign islet adenoma, and

obtained a cure of the hyperinsulinism. After a careful study of these 2 cases, the problem of hyperinsulinism seemed to be solved. Unfortunately it is complicated by our knowledge of the effect of the liver, adrenals, anterior lobe of the pituitary, thyroid, sympathetic nervous system, and possibly other factors on sugar metabolism, particularly their effect upon the development of hypoglycemia. Some believe that other glands of internal secretion exert some regulating mechanism on the activity of islet tissues by means of their secretions. Recently we have learned that hyperthyroidism may be associated with some cases of hyperinsulinism, and a fatal thyroid crises may develop as a complication to the removal of the tumor. Cases showing islet tumors and signs of hyperthyroidism were reported by Aiken (1) and Gilmore and Walton (37). Whipple (82) saw 1 patient die from a postoperative thyroid storm, and 3 other postoperative crises have been reported. In the light of this experience it has been recommended that the basal metabolism rate should be determined in all islet tumor cases, and if it is at all elevated, the operation should be postponed until the patient has been given a course of Lugol's solution, such as we administer preoperatively to a patient suffering from toxic goiter. Hypoglycemia is quite common, but other glands of internal secretion may produce this condition because of some disturbance in the hormonal balance; these should be excluded as much as possible before the opinion is formulated that the hyperinsulinism originated in the pancreas alone.

Three types of anatomical changes in the islets have been reported in hypoglycemia. The first is generalized hypertrophy and hyperplasia; this type is commonly found in infancy, often in the offspring of a diabetic mother, and it responds to suitable dietary measures. The second type is an adenoma of the islands of Langerhans, composed of beta cells; and the third type is carcinoma of the islet cells. Our consideration will be limited to the last two types, as the accepted treatment of these lesions is surgical. Clinically we recognize two types of hyperinsulinism; the type due to an actual islet tumor, and the functional type in which there is little or no alteration of the structure of the islands of Langerhans.

The symptoms most commonly occurring in an attack of hyperinsulinism are: sweating, pallor, tremor, tachycardia, elevation of the blood pressure, fear, mild dyspnea, and severe abdominal pain. Neurological findings are frequently associated with these seizures, the most common being diplopia, dizziness, convulsions, and coma. As the disease progresses, it is not uncommon to find psychiatric manifestations such as emotional instability, disorientation, amnesia, and mania. Attacks of hypoglycemia, as a rule, occur four or more hours after the ingestion of food. They may occur sooner if the patient has undertaken strenuous exercise, thereby increasing metabolic activity and depleting the supply of sugar. Whipple (82), who is one of the most ardent contributors in this field, has given us a characteristic triad of symptoms which he thinks are essential in the diagnosis of an islet adenoma. This triad of symptoms are: (1) attacks of hypoglycemia, however manifested, coming on during the fasting or overfatigued state; (2) associated blood-sugar readings of 50 mgm. per 100 cc. or less during the attacks; and (3) relief of the shock promptly following the ingestion of glucose. Beardwood (8) believes that the glucose tolerance curve is characteristic and of considerable diagnostic value. He points out that it is important for the patient to be on a diet sufficiently high in carbohydrates to avoid any influence that undernutrition might have on the curve, and he also emphasizes that the test should be conducted for six hours. Whipple (82), however, believes that the fasting blood sugar after a twelve- to fifteen-hour fast is a far more reliable test of islet-cell function than is the glucose-tolerance curve. He believes the glucose-tolerance test to be a liver-function test, rather than a test of pancreatic function.

There has been a report (47) of 5 cases of extrapancreatic islet adenoma producing symptoms of hyperinsulinism. We must realize this, when operation is undertaken, as a possibility in cases in which no tumor is found in the pancreas. In 1940 Faust and Mudgett (34) recorded the location of such aberrant tissue in 370 published cases. In 95 instances the pancreatic tissue was found in the stomach, in 105 in the duodenum, in 65 in the jejunum, in 18 in the ileum, and in 49 in diverticuli of the stomach, duodenum, or the small intestine. There are many other localities in which a very small number have been found. An extrapancreatic islet adenoma of the duodenum has been reported with no symptoms of hyperinsulinism. As in other islet tumors, the treatment is surgical. Many contributors have repeatedly emphasized the necessity of complete exposure and palpation of the entire pancreas, including exposure of the head by mobilization of the duodenum. If such an exploration does not reveal a tumor, search should then be made for an adenoma in extrapancreatic tissue, particularly in the sites just mentioned where this tissue is most likely to occur. If no tumor is found, the case should then

be regarded as one of the functional type, and a subtotal pancreatectomy performed. In the early functional cases, partial pancreatectomy was performed with rather discouraging results; however, in 1928 Finney and Finney (35) reported an excellent result following subtotal pancreatectomy, and in 1934 Graham and Hartman (38) reported an excellent result following a subtotal pancreatectomy performed upon an infant. Since these pioneers led the way to subtotal pancreatectomy, many others have reported similar cases, and the results from the more extensive operations have been much more satisfactory and lasting (28).

In hyperinsulinism, the glycogen reserve is frequently used up, and it is well known that any surgical procedure is dangerous if the liver is deficient in glycogen. Guerry and McCutcheon (40) reported a fatality during operation in which there occurred what they termed an operative insulin crisis, even though they safeguarded themselves by having blood-sugar determinations made at the time of the induction of the anesthesia, again when the pancreas was exposed, and also after the resection was completed. In the light of this knowledge and experience, glucose should be administered freely for twenty-four hours before operation, and throughout the surgical procedure. In 1941 Whipple (82) compiled and analyzed 160 hypoglycemic cases that had either been reported in the literature or were reported to him by personal communication. A tumor was found in 136 of these 160 cases; in 107 patients the tumor was found at operation and in 29 it was found at necropsy. The pathological lesion was benign adenoma in 103, questionably malignant adenoma in 22, carcinoma with metastasis in 8, and hamartoma in 1; 2 cases were not differentiated. There were 16 postoperative deaths (15 per cent) among the 107 cases in which a tumor was found at operation. Eight additional deaths occurred after the patients left the hospital; 6 of these patients had carcinoma with metastasis. Bell and Best (10) warned against too extensive a pancreatectomy; they noted that if too much of the pancreas was removed, degenerative changes occurred in the remaining beta cells, and severe diabetes could result. This change is thought to be due to overactivity. This conception is supported by the fact that these degenerative changes do not occur if insulin is administered to the patient.

HYPERPARATHYROIDISM

The parathyroid glands were discovered by Sandstrom in 1880 (72), and in 1900 DeSanti (29) was the first to recognize a tumor of parathyroid origin. The association of parathyroid tumors with the clinical syndrome of von Recklinghausen's disease, generalized osteitis fibrosa, had long been recognized. In some respects this has been a most unfortunate association, as many individuals have generalized osteitis fibrosa cystica or localized cystic changes in bone but do not have hyperparathyroidism. It also focused the attention of most clinicians on the late stages of the disease.

Recently there have been some cases reported in which the patients, which were being treated for stones in the genitourinary tract, and after a careful study of the calcium and phosphorus metabolism were found to have hyperparathyroidism. This does not infer that we should suspect hyperparathyroidism in all cases of kidney stone; on the contrary, it is present in only a very small percentage of these cases. It is evidence, however, that we have become interested in the disease in its earlier stages. The spark which ignited this interest was the report of a cure of the disease following the surgical removal of an enlarged parathyroid gland by Mandel in 1926 (58). Prior to Mandel's case the literature contained scattered reports of parathyroid tumors found at autopsy.

Castleman and Mallory (19) and Albright and his coworkers (2) have made the most exhaustive pathological and clinical studies of the disease. They classified hyperparathyroidism into two types, primary and secondary. The primary types are divided into adenomas, the usual clinical type, and the diffuse type. They pointed out that in the last all parathyroid glands are enlarged. There is a cellular hypertrophy rather than hyperplasia and all the cells are of the Wasserhelle type. Albright (2) reported 6 cases of this type, upon which Churchill had performed a partial parathyroidectomy on all 4 parathyroid glands. This diffuse type of hyperparathyroidism was compared to the diffuse toxic goiter and hyperthyroidism. After these cases were observed for two years, it was apparent that adequate parathyroid tissue was removed, as the increased function of the parathyroid glands was relieved. Other findings, including the amount of tissue to be left, have been included in this study.

In 1905 MacCallum (57) called attention to the fact that renal disease may overshadow the skeletal changes in hyperparathyroidism, when he reported a tumor of the parathyroid gland associated with chronic renal disease. Since that time considerable evidence has been accumulated, indicating that long-standing renal insufficiency may give rise to parathyroid hyperplasia and hyper-

parathyroidism (5). Experimentally, the effect of renal damage on the parathyroids was shown repeatedly. When the renal function is reduced the parathyroids increase in size, and correlated with this, bony lesions comparable to osteitis fibrosa cystica develop. Donahue, Spingarn, and Pappenheimer (30) have demonstrated experimentally that the parathyroid hyperfunction so induced may also in turn have its effect on the kidney. They found that the calcium content of the residual renal tissue was increased in proportion to the parathyroid enlargement. Early removal of the parathyroids prevented this increase in renal calcium. Virchow (79) in 1855 was the first to note metastatic calcification in cases of nephritis, and since that time the association of renal lesions and the deposition of calcium has been reported many times. There are numerous studies demonstrating the frequency with which parathyroid enlargement accompanies long-standing renal disease. To a lesser extent it has been found in rickets, osteomalacia, and pregnancy. Fowweather and Pyreh (36) studied the calcium and phosphorus in 102 cases of renal disease, and found the blood calcium to be over 11 mgm. per 100 cc. in about 50 per cent of the cases. This again points to the danger of attaching too much significance to a single elevation of the blood calcium. It has also been observed that the parathyroids are involved in renal dwarfism.

Langmead and Orr (54) reported a case of renal dwarfism in which the patient died at the age of twenty and in which the skeletal changes were consistent with hyperparathyroidism; four greatly enlarged parathyroids were found at necropsy. The evidence that hyperparathyroidism is an essential part of renal dwarfism appears overwhelming. Parke and Elliot (63) believe that instead of the term "renal rickets" in these cases, the disease should be called "renal hyperparathyroidism with osteitis fibrosa cystica." Elsom, Wood, and Ravdin (32) noted that the renal disease associated with primary hyperparathyroidism has certain clinical features which distinguish it from the usual types of chronic nephritis. Hypertension, cardiac enlargement, edema, and retinal exudates are usually absent or very inconspicuous. Albright and his associates (2) classify the renal lesions associated with hyperparathyroidism as (1) stone formation, (2) parenchymal calcium deposits, and (3) parathyroid poisoning in which there are calcium deposits in the kidney, and, in addition, in other organs such as the lung, stomach, and heart.

Briefly, the clinical findings are divided into three parts: (1) skeletal changes, (2) findings in the genital tract, and (3) a group of general symptoms commonly associated with chronic disease. In addition to these clinical findings we have a disturbance in the calcium and phosphorus metabolism. Typically the blood calcium is elevated, and the blood phosphorus is decreased, and both of these chemical elements are excreted in the urine in greater amounts than they are ingested. Before it is concluded that a patient has hyperparathyroidism we should not forget that many individuals may have at times an elevation in calcium or a fall in phosphorus which has no relation to hyperparathyroidism. A three-day calcium-balance study should be made before any deductions are drawn. By this procedure, we learn that the patient is in a negative calcium balance, and that the direction of flow of calcium in hyperparathyroidism is from the bones to the urine. The calcium-balance study is of paramount importance in early cases, as the clinical findings and metabolic disturbances just enumerated are not as apparent.

Since Mandel's successful cases in 1926, an increasing number of successful cases of parathyroidectomy have been reported in the literature. Unfortunately, parathyroidectomy has been used for lesions other than hyperparathyroidism, such as Paget's disease and hypertrophic arthritis. In these diseases normal parathyroid glands were removed without benefit, and I wish to emphasize again what has been stated before, that it is a very serious mistake to remove normal parathyroid glands, as we have no complete replacement and clinical experience shows that the procedure does not benefit the patient. In any given case of hyperparathyroidism it is important that a careful search be made until the tumor is found. Our surgical experience to date has shown that the parathyroid tumors need not necessarily be found close to the thyroid gland, but may be found in the anterior mediastinum, and as far back as behind the esophagus. It is not difficult to understand the various locations in which the tumors have been found if one studies the anlage of the parathyroid glands (23). Churchill (22), in his report of 30 cases of proved adenoma, mentioned 5 instances in which he found a tumor that had been overlooked at a previous operation. In 1 instance several previous operations had been performed.

Along with the complications which occur in any operation performed upon the neck, tetany is prone to occur after parathyroidectomy. This is in keeping with the insufficiencies observed in operations for hyperfunction of some of the other glands of internal secretion. Of the 30 cases re-

ported by Churchill, 22 developed tetany postoperatively. The tetany was severe in 4, moderate in 3, and slight in the 15 others. When tetany does occur, large doses of calcium, parathormone, and A. T. 10 are the routine therapeutic procedure. The amount and method of administration of these therapeutic agents depend upon the degree of tetany present.

If advanced osteoporosis and cystic disease of the bones are present, many months may elapse before there is much redeposition of calcium in the affected areas. This is easily understood when we realize the small daily intake of calcium in the food. Calcium and vitamin D should be prescribed, and the patient should be encouraged to drink milk and eat cheese or other foods rich in calcium.

TUMORS OF THE ADRENAL GLAND

Tumors of the adrenal gland are difficult to diagnose accurately, and oftentimes are not suspected until discovered at the autopsy table. Although we have known of adrenal tumors since 1765, the first case successfully operated upon was reported by Collett (24) in 1924. There are many types of adrenal tumors, but our primary interest in this discussion will be focused upon the cortical and medullary tumors which produce metabolic changes. In 1927 (76) extracts of the adrenal cortex were prepared which would prolong the life of adrenalectomized animals. This was of immeasurable value as it gave the surgeon a therapeutic agent which would combat the frequent and highly fatal postoperative complication of acute adrenal insufficiency. Since then, many observations and contributions have been made concerning the chemistry, physiology, and clinical diagnosis associated with these tumors.

TUMORS OF THE ADRENAL CORTEX

The symptoms of cortical tumors of the adrenal gland are in no way constant. They are dependent upon the age of the patient, the sex of the patient at the onset of the illness, the degree of endocrine activity of the tumor, and the duration of the disease. A study of the reported cases shows that the cortical tumors occur most frequently in young women, although they have occurred in young children. When the tumor develops in a child, precocious puberty usually occurs. In boys the precocious puberty is masculine in type, in girls it is heterologous. The most common findings indicating precocious puberty in girls are hypertrophy of the clitoris, deepening of the voice, masculine distribution of the hair, and occasionally precocious menstruation. One case has been reported (80) in which a child of two had two or three menstrual periods. When a cortical tumor occurs in an adult, virilism develops in the female, and feminism in the male. The most frequent evidences of virilism in the female are growth of hair in the masculine distribution, the growth of a beard and mustache, atrophy of the breasts, masculine habitus, cessation of the menses, atrophy of the reproductive organs, and hypertrophy of the clitoris. In the male the most common evidences of feminism are atrophy of the penis and testes, and enlargement of the breasts.

Clinically, in addition to these changes in sex characteristics, the patients frequently develop the symptoms and clinical findings associated with Cushing's syndrome of basophilic adenoma; namely, obesity or a change in the distribution of the fat, hypertension, osteoporosis, purple striations of the skin, acne, polycythemia, frank diabetes or changes in the carbohydrate metabolism, and fatigue. If the tumor is large enough, local symptoms may develop which are characteristic of any other abdominal tumor of the same location. Any of these symptoms just enumerated may or may not be present in a given case. Any or all have been absent, and almost every combination of them have been found in individual cases. Closely related both to a tumor of the adrenal cortex and to Cushing's disease is a condition which frequently has been referred to as adrenocortical "hyperplasia." This has been found at autopsy in an appreciable number of proved cases of Cushing's disease, and in another group of cases, in which the clinical picture is compatible with the diagnosis either of adrenocortical tumor or of basophilic adenoma of the pituitary body. Cushing's syndrome may be associated with tumors of the thymus, enlargement of the parathyroid glands, and arrhenoblastoma of the ovary, in addition to basophilic adenoma and adrenocortical tumor. It is commonly believed that the hyperfunctioning basophilic tumor of the pituitary gland may stimulate overactivity of the adrenal cortex. There is some experimental work to indicate that such might be the case. Evans (50), and Collip and his associates (26) have independently presented evidence indicating the existence of adrenotropic hormones. Smith (75) also demonstrated that removal of the pituitary gland greatly decreased the size of the adrenal glands and was associated with atrophy and vascular degeneration of the cortex, and that the administration of an extract of the anterior lobe of the pituitary gland produced marked hypertrophy of the cortex. Evans concluded that the adrenocortical tissue needs for its normal function

some constituent of the anterior lobe of the pituitary gland. Cecil (20) reviewed the literature and noted that in 30 per cent of the reported cases of cortical tumor, the adrenal gland opposite to the one occupied by the tumor was absent or inadequate to support life. Ingle and Kendall (49) supported Cecil's findings by noting that the administration of large amounts of cortin produced atrophy of the adrenal cortex of the rat, but if the adrenotropic hormone was administered with cortin, the degree of atrophy was but slight.

Minor disturbances in the carbohydrate metabolism are found frequently in patients with a tumor of the adrenal cortex. However, in 1939 Shepardson and Shapiro (74), in a careful search of the literature, could find only 17 proved cases of adrenocortical tumor associated with diabetes, and added 1 of their own. Lukens, Flippen, and Thigpen (56) reviewed the status of the carbohydrate metabolism in 44 cases of cortical tumors and 11 cases of bilateral adrenocortical hyperplasia reported from 1917 to 1935. There were no disturbances in the carbohydrate metabolism in 24 cases of tumor and in 4 cases of hyperplasia; but there were transitory glycosuria in 4 cases of tumor and 1 case of hyperplasia, and marked glycosuria in 13 cases of tumor and 6 cases of hyperplasia. On the basis of the clinical and experimental evidence, there is considerable doubt that the adrenal cortex is responsible for this carbohydrate imbalance.

Many believe that the greatest recent advance in the diagnosis of hyperfunctioning lesions of the adrenal cortex has been the clinical application of assays of the urine for hormonal-like substances. Cahill (16) classifies cortical tumors on the basis of the presence or absence of these hormonelike substances. He has observed that tumors with no recognizable hormonal changes occur infrequently, usually in patients over thirty years of age, and in either sex. As a rule these tumors have been present for a long time without symptoms, and the prognosis is very poor as they are not diagnosed until late. The tumor is suspected and located very frequently because the patient complains of local symptoms which are due to the tumor, such as abdominal pain or pain in the flank of the affected side which is made worse by exercise.

Perhaps a contribution of greater value in the diagnosis of adrenocortical tumors is the quantitative determinations of neutral 17 ketosteroid in urinary assays. Extensive investigation in this field has been carried out by Callow (17) and Talbot (77) and their associates. Only a few months ago, Talbot concluded that the urinary 17-ketosteroid measurement has earned a place among those clinical laboratory procedures which provide diagnostic information. Determination of the output of the 17 ketosteroid is helpful in detecting both hyperfunction and hypofunction of the adrenal cortex, and hypofunction of the thyroid and pituitary glands. The output is markedly lowered in diminished function of the adrenal, thyroid, and pituitary glands; there is marked increase of excretion in hyperfunction of the adrenal cortex, but increased function of the thyroid or pituitary does not cause a significant elevation in excretion.

It has been shown that the 17 ketosteroid found in the urine is derived from the adrenal cortex and the gonads. This is not difficult to understand when we realize that both of these tissues have their anlage in the genital ridge. Further studies showed that the normal value of the 17 ketosteroid drops one-third in castrated subjects. From this we can deduce that two-thirds of the 17 ketosteroid comes from the adrenal cortex, and one-third from the gonads. The normal amount of the 17 ketosteroid found in the twenty-four-hour specimen of urine depends upon the age of the individual. The normal amount for a child up to ten years of age is 1 mgm. At puberty the amount varies with the sex of the individual: in the male from 10 to 20 mgm. is normal, whereas in the female the normal is from 9 to 15 mgm. If the determination of the 17 ketosteroid is 30 mgm. or over, it is almost certain to be due to an adrenocortical carcinoma. This was first observed by Callow and has been confirmed by Hoffman and many others. If the 17 ketosteroid is increased, although below 30, it is impossible to say whether it is due to simple diffuse hyperplasia or a nodular hyperplasia of the adrenal gland. If there is evidence of associated hyperpituitarism, the likelihood is that it is a hyperplasia. In the presence of a feminizing tumor of the male adrenal cortex there is no increase in the 17 ketosteroids, but estrogenic substances are increased. Based on the significance of the 17-ketosteroid determinations, the following functional classification (Table II) was developed by Hoffman (46) while working in the laboratories of Custer.

As an aid to diagnosis, Carrelli (18) in 1901 demonstrated that carbon dioxide infiltrated into the perirenal fascia would be of value in the visualization of the kidney capsule and the adrenal gland by x-rays. Oftentimes, because of the rapid diffusion of the carbon dioxide, it was difficult to demonstrate the outline of the adrenal gland. In 1935 Cahill (15) reported the use of a

measured amount of air injected directly into the perirenal space by hand pressure. He took roentgenograms shortly after completion of the injection, and at twelve, eighteen, twenty-four, and thirty-six hours after the injection, and found the organs and fascial planes to stand out very clearly, especially, as desired, around the adrenal gland. Accidents have occurred in the use of this diagnostic procedure, and this danger must be considered before an air injection is undertaken. Recently, Pendergrass (64) has reverted to Carrelli's original idea of the use of carbon dioxide in obtaining the roentgenogram of the adrenal glands. This gas is less dangerous, is absorbed rapidly should it be introduced into the blood stream, and, therefore, eliminates the dangers of air embolism and its sequelae. Intravenous urography should be included in the routine studies. If a tumor is present it demonstrates that the kidney is pushed down on the affected side.

All agree that the proper treatment of an adrenocortical tumor is surgical. It has been suggested that the adrenal gland should be explored in all cases of Cushing's syndrome lest we miss an opportunity to operate upon a cortical tumor early. Several surgical approaches have been advocated, the transthoracic, the posterior kidney incision, and an abdominal incision. The last two are used by the vast majority of surgeons. It seems to me that when we carefully consider all the factors, the abdominal approach is the most desirable. It has most of the advantages that the kidney incision affords the surgeon, and in addition both adrenal glands may be palpated through this incision before the tumor is removed. This, I think, is of great importance especially since Cecil found the opposite adrenal gland to be absent or inadequate to support life in 30 per cent of the reported cases. The condition of both adrenal glands should be noted before removal of the tumor, so that we may anticipate the development of postoperative adrenocortical insufficiency. Also, by the abdominal approach the pelvic organs may be explored in the female to determine whether or not an arrhenoblastoma of the ovary, or, more rarely, a granulosa tumor is present. The operative mortality in cortical tumors is quite high, practically 50 per cent in the reported cases. Lukens *et al.* (56) collected from the literature 40 cases of this type of tumor which had been operated upon, 19 of which terminated fatally. The most common complication following operation is adrenocortical insufficiency. This was responsible for the almost prohibitive mortality; however, recently a routine has been developed for the management of this complication which has proved very satisfactory, and has permitted us to carry the patient over the period of acute insufficiency until the remaining adrenal tissue could undergo sufficient hyperplasia to compensate for the loss of the other adrenal gland and produce adequate adrenal secretion to maintain life. The treatment of this complication is the same as is used when it occurs in Addison's disease; namely, the administration of adrenocortical extract, the sodium ion in the form of sodium chloride and sodium citrate, adequate doses of vitamin C to fix the salt, and a diet low in potassium. Walters (80) believes that we should anticipate postoperative adrenal insufficiency, and institute this treatment throughout the postoperative period. The patient should be watched carefully for any premonitory signs of acute adrenal failure. The more important symptoms of this complication are nausea, vomiting, weakness, a rapid weak pulse, and falling blood pressure. More recently, with the exception of the administration of the adrenocortical extract, the same regime has been used for a few days before operation. In reporting 8 cases operated upon for cortical tumor, Walters states that he had 7 consecutive successful results, the 1 fatality having occurred in 1924 before we knew how to control adrenal insufficiency adequately.

TABLE II.—DYSCRASIAS OF THE ADRENAL CORTEX
FUNCTIONAL CLASSIFICATIONS

	Neutral 17 ketosteroids
1. Hypercorticalism	
Primary	
a. Adrenocortical carcinoma	++++
b. Diffuse hyperplasia	+++
c. Nodular	++
d. Feminizing tumor of the adrenal cortex (6 cases); estrogen increased	o
Secondary	
a. Hyperplasia secondary to hyperpituitarism, i.e., certain types of Cushing's syndrome	++
b. Secondary adrenocortical carcinoma associated with Cushing's syndrome	+++—++++
2. Abberrant corticalism (steroids of unusual types)	
3. Hypocorticalism	
a. Adenoma	(— —) to (o)
b. Hypoplasia	—
4. Tumors of nonglandular epithelial origin	

MEDULLARY ADRENAL-GLAND TUMORS

Medullary tumors of the adrenal gland have been observed for many years, but the surgical removal of these lesions is a comparatively recent adventure. In 1927 C. H. Mayo (59) reported the

first successful removal of such a tumor. He called attention to the fact that the patient developed severe adrenal insufficiency in the course of the operation, and heroic measures, large doses of adrenalin, were necessary to keep the patient from dying on the operating table. This experience is a common one to surgeons operating upon patients with medullary tumors of the adrenal gland.

There are three pathological types of medullary tumors according to the type of cell from which they are derived: (1) sympathoblastomas from embryonic cells, (2) ganglioneuromas from mature ganglion cells, and (3) pheochromocytomas, or paragangliomas, from mature chromaffin cells. It is the last type in which we are interested as this is the only type which, it is thought, can produce epinephrine.

Clinically, the patient suffering from a pheochromocytoma is subject to paroxysms of hypertension at various intervals. The longer the patient's history, the briefer is the interval between paroxysms, and in some of the oldest cases the hypertension has become constant. The most common symptoms associated with these attacks of paroxysmal hypertension are pectoral pain, tachycardia, pallor and flushing, the sensation of cold followed by heat, profuse sweating, and nausea and vomiting. The majority, but not necessarily all of the symptoms occur in all cases. In the past few years, some cases have been reported in which patients suffering from pheochromocytomas have also presented the clinical picture of hyperthyroidism. McCullagh and Engle (60) gave a very complete report of 2 such cases, and in 1 of their cases a thyroidectomy was performed with no relief, and a subsequent removal of the medullary tumor resulted in complete abatement of the symptoms, including those of hyperthyroidism. The basal metabolic rate, which had been moderately elevated, was unaffected by the thyroidectomy and returned to normal following the removal of the medullary tumor. These cases again illustrated how confusing the symptomatology may be in the presence of increased function of the adrenal and thyroid glands. Cases have been reported in which massage over the tumor in the course of the physical examination produced a sharp rise in the blood pressure. Crane (27) reported a case in which this clinical finding was the most important factor in enabling him to diagnose the presence of a medullary tumor. While this may be very valuable in assisting one in arriving at the diagnosis, palpation of these tumors is not without danger, and sudden deaths have been reported following too vigorous palpation of a pheochromocytoma.

The diagnosis of medullary tumors is quite difficult. As a rule the patients have to be observed and studied in their paroxysms of hypertension before this lesion is considered. If the disease has progressed until the hypertension is constant, the problem becomes all the more difficult. As in the cortical tumor, the perirenal injection of air is of diagnostic value; however, it must be realized that at times these tumors are very small, and if the clinical picture leads one to suspect such a tumor, failure to find any enlargement of the adrenal gland as outlined by the injected air is no contraindication to surgical exploration.

Experience with these tumors is very limited; in 1940 Brunschwig and Humphreys (14) were able to find only 103 cases in the literature, most of which were found at autopsy. The treatment of medullary tumors is surgical. It is extremely hazardous to operate upon these patients, and death during the course of the operation is not infrequent from acute vasomotor collapse associated with hyperactivity of the tumor. Brunschwig and Humphreys pointed out the frequency with which this complication occurs in the clinical course of the patient and emphasized the importance of prompt diagnosis and treatment lest the patient die of a fatal attack. Not infrequently patients with medullary tumors have succumbed to minor surgical procedures performed elsewhere in the body. Here again the abdominal approach is thought to be the best, as the vascular pedicle to the tumor may be clamped and tied before the gland is manipulated. This prevents the squeezing of excessive quantities of adrenalin into the circulation. In 1941 Biskand, Meyer, and Beadner (11) were able to find 29 reported cases which had been operated upon. They noted that the lesion was more common in females than in males, was more frequent on the right side than on the left, and was extrarenal in 4 instances. Eighteen patients developed acute adrenal insufficiency and 4 died immediately after the operation. Fifteen patients were followed up; 12 were symptom-free, 2 were alive with slight symptoms and blood-pressure variations, and 1 had died. Fortunately this lesion is rare, as the clinical outlook is very discouraging.

SUMMARY

With increased experience in the field of metabolic diseases, the multiplicity of glandular involvement in patients presenting metabolic problems has become more apparent as the complexity of these syndromes unfolds. Great progress has

been made in establishing therapeutic measures aimed to prevent, as well as to treat successfully the insufficiencies which are so prone to develop in operations performed upon the glands of internal secretion. There are many phases of these diseases with which the surgeon could not hope to familiarize himself to the degree that the metabolist or the clinical pathologist does. This being the case, all patients who have surgical lesions with metabolic changes require the closest supervision and study by the internist and surgeon. One need only look at the progress made in surgery of the diabetic by this combined management to appreciate its full significance. In some fields, such as surgery in hyperinsulinism and hyperparathyroidism, we have a great deal to learn in diagnosis as well as in treatment. There are those who feel that there are unlimited possibilities in the future of surgery upon the adrenal gland. Many intricate diagnostic problems and surgical complications which occur in surgery in metabolic diseases are entirely foreign to other types of general surgery. Today many institutions have a department of metabolic disease in the medical division, and should have a similar department in the surgical division. By the close co-operation of these two departments, we would be able to diagnose and treat more satisfactorily, patients suffering from metabolic diseases which require surgical treatment, and thereby improve our operative results, and lower our operative mortality.

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Brunner, H.: Chronic Osteomyelitis of the Skull. *Ann. Otol. Rhinol.*, 1943, 52: 850.

The author presents an exhaustive study of both primary and secondary chronic osteomyelitis of the skull.

Primary chronic type. Acute infection of the paranasal sinuses is less important as an etiological factor in this type of osteomyelitis than it is in acute osteomyelitis. Staphylococci play a similar role as in the acute type, but the author points out that cultures were frequently sterile. Anaerobic bacteria may play an important part. The clinical course is chiefly characterized by an insiduous onset and by the poorly marked tendency to spread. Pathology in the nose was found if the disease originated in the paranasal sinuses or if these spaces were involved secondarily. Evidence is presented which seems to show that chronic osteomyelitis of the primary type generally develops in the anterior wall of the frontal sinus. X-ray study shows the outlines of the sinus to be indistinct or absent, and that the sinus may be replaced in some cases by a sclerotic area ending abruptly in the midline of the frontal area.

As to treatment, if the frontal sinus is not involved, any sequestrum that forms should be removed. If the frontal sinus is involved, the Riedel or Kuhnt operation should be performed. Bacteriological data show that hemolytic streptococci and staphylococci were found; these are also found in acute osteomyelitis.

Secondary chronic type. This is chiefly characterized by its acute onset, its marked tendency to spread within the bone, and its marked tendency to spread within the blood, i.e., to produce chronic septicemia.

In all the presented instances the disease set in with the typical symptoms of an acute osteomyelitis. However, the onset was not followed by a constant progress toward the vault of the skull and a progressive destruction of bone, nor by a self-limited course leading to the formation of one single sequestrum without further symptoms of progress, nor by a brain abscess or a fulminating meningitis.

In these cases the acute osteomyelitis gradually turned into a chronic osteomyelitis which was definitely progressive. However, the progress was extremely slow, extending over a period of years, and did not consist primarily of destruction of bone; rather, it consisted of the formation of new bone leading to a thickening and sclerosis of the vault, of the malar bone, and of the wings of the sphenoid, and, to a lesser degree, to the formation of sequestra, which was probably due to an obliteration of the blood vessels. There were always multiple sequestra (in contradistinction to the self-limited type of acute osteomyelitis) which frequently contained parts of the lamina externa and of the diploe of the bones of the skull, but which did not produce penetrating defects of the bones of the vault.

The most important feature was the chronic septicemia, characterized by the appearance of metastases. There were no marked changes of the blood or of the spleen. Study of the x-ray films seemed to indicate that the pathology is very similar to that of chronic osteomyelitis of the primary type. The infection in both types produces osteoclasis and osteogenesis, the latter being predominant. Because of these changes, thickening and sclerosis is found, on the one hand, and sequestra, on the other. However, there are some points of difference between chronic osteomyelitis of the primary and secondary types. While in the former the sclerosis is to be found in the boundaries of the frontal sinus and spreads extremely slowly into the surrounding parts, in the latter the frontal sinus may regain its normal appearance and the sclerosis and the sequestra are to be found in the distant parts of the skull, as in the vault or in the malar bone, or in the wings of the sphenoid. Therefore, in instances in which an x-ray film is taken several years after the onset of the condition, the boundaries of the frontal sinus may appear distinct, although the disease undoubtedly originated in the frontal sinus.

The treatment of these cases is extremely unsatisfactory. There are a chronic septicemia, a widespread osteomyelitis, and, as a rule, metastases, which may eventually also serve as the origin of septicemia. It is obvious that under these circumstances surgery cannot accomplish very much. At present, the best treatment consists in preventing the change of the acute osteomyelitis into the chronic form. This can be accomplished only by radical treatment of the acute osteomyelitis.

J. M. MORA, M.D.

Smith, F.: Planning the Reconstruction. *Surgery*, 1944, 15: 1.

The purpose of all reconstructive surgery is the restoration of the part or area to normal, or as near normal as possible. This should include both function and cosmesis. The relative importance of these two objectives varies with the area that is being repaired. The principles of reconstruction of all body surfaces, whether the condition is the result of trauma, or burns, or a congenital defect, are the same, but in defects of the face and neck, the principles of surgical repair are most exacting to meet the dual purpose of the effort. All the required mate-

rials for the repair with two exceptions (cartilage and cornea), are available in the patient's body, and their use is vital to a successful ultimate outcome.

In planning a reconstruction, the surgeon must thoroughly consider the possibility of utilizing tissue from the neighborhood of the defect and of transferring it in one of the several ways available, before giving consideration to the procedures so universally employed in recent years. The employment of the principles of Z plastic, multiple excision, and interpolated flaps from the vicinity of the defect should have first consideration in the planning of a correction, whenever the surgeon may choose his procedure.

The evolution of modern practice in facial repair has been profoundly influenced by the popularization of tubed pedicle flaps, free grafts, and rotated flaps from the forehead. Reconstructions using these methods, however, are procedures of necessity rather than of choice. A better understanding of the varied uses of Z plastics, the employment of the principle of multiple excision, and the use of flaps of normal tissue from the vicinity of the deformity will greatly improve the end-results.

SAMUEL KAHN, M.D.

Davis, W. B.: Some Deformities of the Face and Their Correction. *Surgery*, 1944, 15: 43.

Facial deformities assume importance from several viewpoints: namely, functional, psychological, cosmetic, vocational, and economic. Their correction has received periodic attention since early authentic surgical history. Rhinoplasties were done in India as early as 1000 B.C., and later in Italy.

Pigmented nevi may be major disfigurements, sufficient to exert dominant influences upon an individual's mental attitude, and upon the social and economic outlook. Fortunately, most of them are amenable to surgical measures which make the areas relatively inconspicuous. Whenever possible, excision and advancement of the surrounding skin should be the method of choice, since skin grafted from some distant donor site never has exactly the same color and texture as that of the adjoining skin. However, grafts from distant areas are necessary in many cases.

Marked congenital deficiencies of the nasal bones and of the frontonasal processes of the maxillae are preferably corrected between the ages of seventeen and twenty years by autogenous rib-cartilage transplants. If correction is attempted in childhood the transplanted cartilage usually does not increase enough in size and, consequently, as maturity is approached there is a disproportion between the size of the transplanted cartilage and the size of the developed face. If, in some cases, early correction is deemed advisable because of psychological reasons, the patients and their parents should be told that a second operation may be necessary during late adolescence.

Excess convexities of the dorsum nasi are usually associated with some elongation and drooping of the nasal tip. Corrections are made by freeing the overlying skin and subcutaneous tissues from the cartilagenous bridge, and the periosteum from the bone to be removed, through an incision made within the superior portion of the anterior nares. In most instances it is preferable to remove the excess convexity by means of numerous rasps in assorted shapes and sizes. In some instances saws are preferred for removing very large humps. If the width of the new dorsum is too great, the frontonasal processes may be divided with a saw or narrow chisel, near their attachment to the bodies of the maxillae, and then pressed medially to the desired width. After the columella is freed from its attachment to the septal cartilage by a through-and-through incision, a triangular section of the cartilage of the necessary size to secure the desired degree of shortening is removed and the columella is then sutured to the septum in the position which properly elevates the tip.

In the author's series cavernous hemangiomatous areas about the lips, eyelids, or cheeks which are primarily treated surgically by excision and plastic reconstruction have shown better cosmetic results, especially in adults, than those treated by radiation alone, or by radiation followed by plastic repair. In the cases in which the eyelids are involved, adequate radiation probably would carry with it some risk of damage to the eyball structures.

LOUIS T. BYARS, M.D.

Ivy, R. H.: The Repair of Bony and Contour Deformities of the Face. *Surgery*, 1944, 15: 56.

Displacement or loss of supporting structure of various parts of the face as a result of faulty development, injury, disease, or operation is accompanied by impairment of function and appearance. Acquired deformities involve displacement or loss of supporting tissues (bone and cartilage), as well as of overlying soft tissues, of varying extent, which cause cosmetic or functional disturbance or both.

After a fracture of the mandible, with or without loss of substance, union may take place with shortening at the site of fracture and result in facial asymmetry and functional disturbance. The same sort of deformity may follow loss of a portion of the mandible from necrosis or operation for removal of a neoplasm. Here, the displacement must first be corrected by osteotomy at the site of malunion or by division of the adhesions holding the displaced fragments in a contracted position, and by the reduction of fragments to a position as normal as possible, followed later by bone grafting if a gap remains that is too wide to be bridged by spontaneous bone regeneration.

The object of treatment in patients with loss of substance of the mandible from whatever cause is primarily restoration of the function of mastication. This is attained by restoring the normal occlusion of the remaining teeth and stabilizing the jaw by filling in the lost continuity of the bone. A secondary objective is the building out of contour of the face for improvement in appearance. In patients with loss

of substance it is very rarely desirable to obtain union by bringing the ends of the fragments together and sacrificing the occlusion of the teeth. This results in a crippling of the masticatory function and an increase in the external deformity.

In nearly all cases of this type the preliminary operation requires cutting through the oral mucosa, which makes it absolutely necessary to postpone the bone grafting until complete healing has occurred.

During the past twenty-four years the author has limited himself to two types of bone grafts, each having fairly definite indications; namely, the osteoperiosteal graft from the tibia and the graft from the crest of the ilium.

Exposure and preparation of the mandibular fragments are done before removal of the graft from the donor site in order that the size of the graft required may be determined, and also on account of the possibility of entering the mouth while preparation of the bed for the graft is being made, an accident that would render the application of the graft useless at this time. Another reason for this order of procedure is the desirability of protecting the viability of the graft by placing it in its new position as soon as possible after removal from its original site. Postoperatively, fixation of the jaws must be maintained until consolidation is well advanced; that is, for at least eight weeks. Regeneration may be checked by x-ray examination at monthly intervals, but the final test of consolidation is by clinical examination after the upper and lower teeth are disconnected.

LOUIS T. BYARS, M.D.

Thoma, K. H.: Eosinophilic Granuloma With Report of 1 Case Involving First the Mandible, Later Other Bones, and Accompanied by Diabetes Insipidus. *Am. J. Orthodont.*, 1943, 29: 641.

This condition, first described as an independent new disease and named solitary or eosinophilic granuloma by Otani and Ehrlich in 1940 and by Lichtenstein and Jaffe also in 1940, was believed by Farber, in 1941, to be closely related to Schueller-Christian's disease and Letterer-Siwe's disease.

Fig. 1. Left mandible, taken in December, 1942.

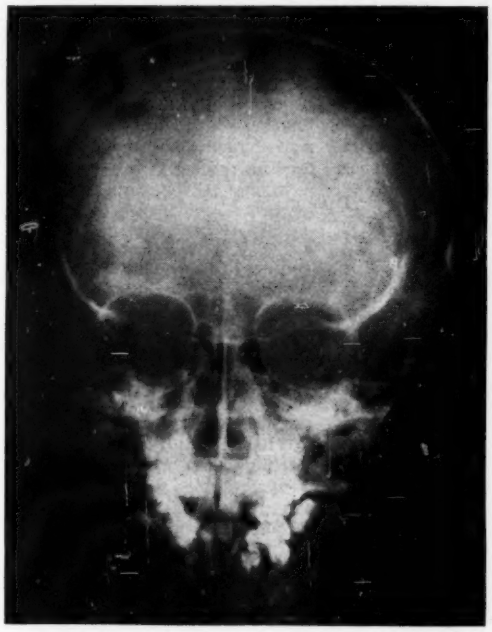


Fig. 2. Roentgenogram of skull, taken in December, 1942.

The roentgen appearance of the lesions varies in contour, being round, oval, or irregular in outline. The lesions give a punched-out effect, and do not expand the cortex, although, on occasion, they erode through it. There are unusual reactive changes in the bone itself, except in the healing phase. The areas often develop very rapidly, and, frequently, heal equally rapidly after roentgenotherapy.

The causative factor is unknown. The disease in the case reported was associated with diabetes insipidus, which was not found in cases previously reported by Farber, Mallory, Lichtenstein, and Jaffe. This, therefore, links the disease still more strongly with Schueller-Christian's disease.

There are no consistent differential diagnostic laboratory findings.

The destructive lesion in bone, Farber writes, is essentially a granulomatous one, with variations which appear to depend on the duration of this granulomatous process; eosinophilic infiltration is frequently, but not always, a prominent feature. The eosinophils may be either mature leucocytes or eosinophilic myelocytes gathered in clumps or scattered diffusely through the section; they contain variable numbers of plasma cells, lymphocytes, and polymorphonuclear leucocytes unassociated with bacterial infection. Giant cells are common.

These lesions respond to roentgen treatment administered in relatively small doses. Some lesions

also heal following partial excision and curettage, or a combination of the two.

Prognosis should be guarded. In the series of Green and Farber, 9 of the 10 patients were well on the follow-up, but 1 had died and details were not available. The termination of the disease is uncertain.

A detailed case report including roentgenograms, photographs, and photomicrographs is presented.

ROBERT P. MONTGOMERY, M.D.

EYE

Pfeiffer, R. L.: Traumatic Enophthalmos. *Arch. Ophth.*, Chic., 1943, 30: 718.

The author states that enophthalmos following trauma is always indicative of fracture (usually of the floor) of the orbit. Displacement of the eyeball results from fragmentation of the floor of the orbit with prolapse of the orbital contents into the antrum, and fracture of the lamina papyracea with compression of the ethmoid cells. The author reports that enophthalmos appeared in 53 of 120 cases of fracture of the bones of the face associated with involvement of the orbit, and that fracture was present in every case of traumatic enophthalmos observed during a period of ten years.

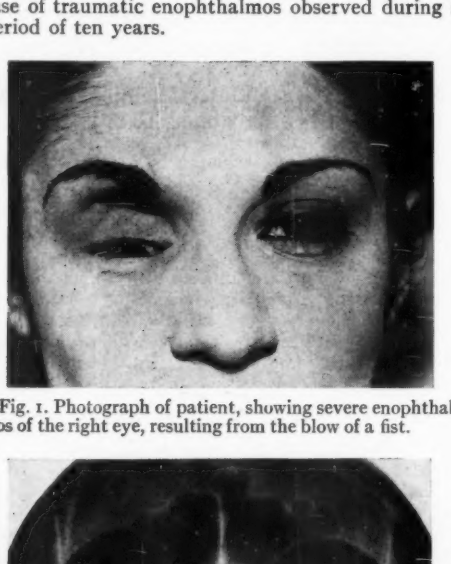


Fig. 1. Photograph of patient, showing severe enophthalmos of the right eye, resulting from the blow of a fist.

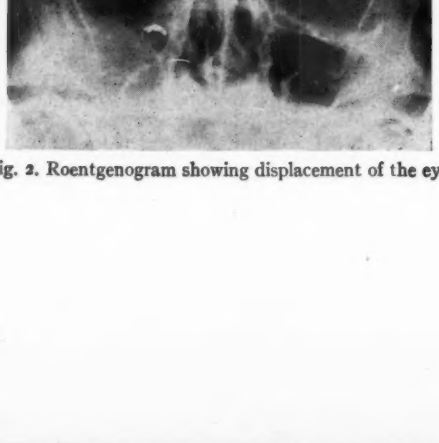


Fig. 2. Roentgenogram showing displacement of the eye

Fracture of the floor of the orbit can be recognized in roentgenograms of the skull in the Caldwell position; prolapse into the antrum, in the Water position.

The deformity may be corrected by reconstruction of the floor of the orbit with autogenous tissue, bone or cartilage, to create a new floor, or with fat to fill the antrum in order to elevate the eyeball and orbital tissues. Roentgenographic examination is advocated in all cases of recent injury to the eye associated with fracture of the orbit.

JOSHUA ZUCKERMAN, M.D.

EAR

Conley, J. J.: Analysis of 100 Consecutive Cases of Aural Disease in an Army General Hospital. *Arch. Otolar.*, Chic., 1943, 38: 541.

An analysis of the first 100 cases of aural disease admitted to the Tilton General Hospital, New Jersey, is presented with reference to the cause and treatment of the condition, and the disposition of the patients. Approximately 4.3 per cent of the first 2,290 patients admitted for all causes had aural disease. Seventy-seven per cent of the patients with aural disease had a suppurative condition. Eighty-five per cent presented some type and degree of deafness. Thirty-three per cent underwent some form of surgical intervention. Approximately 75 per cent of these men with disease of the ear were held for limited or full duty. NOAH D. FABRICANT, M.D.

NOSE AND SINUSES

McNally, W. J., Stuart, E. A., and Childe, A. E.: Mucocele of the Frontal Sinus: A Report of 5 Cases, in 2 of Which at Operation the Mucocele Was Found to be Empty. *Arch. Otolar.*, Chic., 1943, 38: 574.

The unusual circumstance with regard to 5 cases reported as mucocele is that in 2 the mucocele was found to be empty at operation. These cases have been classed as mucocele because of the fact that it would be impossible to explain the findings in any other way. There is no clinical method other than operation for determining whether or not such a sinus is empty. An external exploration of the sinus is more likely to insure permanent intranasal drainage.

Conditions which are most likely to be confused with mucocele are: pyocele, cyst (such as hydatid cyst), and epidermoid. The distinction can be made only by operation, and the operative treatment, viz., permanent and free intranasal drainage, is the same in all of these conditions. Roentgenograms are valuable in diagnosis. NOAH D. FABRICANT, M.D.

NECK

Simpson, W. L., and Graham, D. G.: Injuries of the Cervical Thoracic Duct. *Ann. Otol. Rhinol.*, 1943, 52: 834.

At the root of the neck, on the left side, opposite the lowest cervical vertebrae, the thoracic duct

arches laterally above the apex of the pleural sac and then downward and forward across the first part of the subclavian artery. It passes in front of the vertebral artery and vein, the thyrocervical axis, the medial border of the scalenus anticus, and the left phrenic nerve, and behind the left carotid sheath and its contents. It ends by joining the left innominate vein in the angle of the junction of the internal jugular and the left subclavian veins.

The symptom of injury to the cervical portion of the duct is a flow of milklike fluid from the site of injury. When the fistula is complete, the volume of fluid lost is very large, as much as several pints daily. This dehydration produces excessive thirst and decreases the urinary output, and the skin becomes dry.

If the duct is injured during an operative procedure it may be ligated successfully or a laceration may be sutured laterally. If the duct is injured by an external penetrating wound, or the injury is not recognized during surgery, no effort should be made to implant the duct into a vein, as has been done immediately following the severance of a duct during surgery.

When secondary ligation, closure, or repair is undertaken, a fat meal should be given one hour prior to such a procedure. This insures a distinct milklike flow of chyle which will aid materially in the visualization of the duct. The preoperative administration of morphine is contraindicated, as this markedly decreases the flow of chyle.

The author reports a case of severed thoracic duct due to a gunshot wound. Packing failed to close the duct. The fistulous tract was dissected down to the duct and ligated. The ligature slipped off four days later; then double ligation was done and the adjacent tissues were sutured over the wound. Sulfanilamide powder was dusted into the wound, which was then tightly closed. This procedure was followed by firm healing.

The patient had generalized cramplike abdominal discomfort following meals during the first two weeks after operation, but this symptom gradually subsided. The patient regained her normal weight and health.

EARL O. LATIMER, M.D.

Campbell, A. A.: Cancer of the Larynx. *Canad. M. Ass. J.*, 1943, 49: 509.

In a series of 103 cases of cancer of the larynx, the disease occurred between the ages of fifty and seventy in two-thirds of the patients and was six times as frequent in males as in females. A comparison of two five-year periods fifteen years apart shows that the incidence of cancer of the larynx has not changed. The classification by Krishauber of carcinoma of the larynx into intrinsic and extrinsic types is of clinical value, the false cord being the point of differentiation. Lesions below this line, including subglottic growths, are classed as intrinsic. The carcinoma was of the epidermoid type in all cases. The only subclassification suggested by the pathologist was that of differentiating or nondifferentiating cell types. Constant and persistent hoarseness was the most common initial complaint. Extrinsic types were often advanced before any symptoms were noted and large glands in the neck were the first indication in 6 cases.

Suspension laryngoscopy under general anesthesia is recommended for diagnosis and biopsy. Treatment must be radical. Radiation therapy is now worthy of consideration in all cases, but those cases which are most suitable for operation seem also to be the most suitable for irradiation. If one fails, the other is likely to fail. The two treatments are not complementary and combined treatment does not seem to improve results. In late cases irradiation has much to offer in the way of palliation.

Of 103 patients, 9 were considered suitable for laryngofissure, and 4 of 8 patients who were operated upon were cured. Laryngectomy was done in the cases of 5 patients, 3 of whom were cured for periods of five years or more. Early cases of cancer of the larynx, with the growth restricted to one cord or extending to a limited degree on the anterior end of the opposite cord, would be considered most favorable for irradiation, but since the effect of irradiation is more difficult to prognosticate than that of laryngofissure, the latter procedure is recommended in all suitable cases. The author believes that laryngectomy is rapidly becoming an obsolete operation.

JOHN R. LINDSAY, M.D.

SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Brenner, C., and Cohen, S.: The Effect of Certain Sulfonamides on the Electrical Activity of the Cerebral Cortex. *J. Am. M. Ass.*, 1943, 123: 948.

Because of the increase in bullet wounds and injuries of the head during wartime, and the use of sulfonamides in other parts of the body under such circumstances, this article is of some interest. It has been known for a considerable length of time that certain sulfonamides are poorly tolerated when in contact with the brain; they may cause convulsive seizures. This is true particularly of sulfathiazole. Therefore, experiments were conducted with a view to determining the effect of the local application of these drugs, and, especially, the electrical activity of the cortex.

The experiments were done on 23 cats. Sodium sulfanilamide was tested 8 times; experiments were conducted with both soluble and insoluble preparations. It was found that the direct application of sulfathiazole, or of a solution of the sodium salts of sulfathiazole, or of sulfapyridine or sulfadiazine, to the cat's cortex gives rise to spontaneous electrical activity in the cortex, which appears in the electroencephalographic records as high-voltage spike discharges and is to be regarded as a convulsive state of the cortex. The results with sulfanilamide were different. Neither the drug itself nor solutions of its sodium salt, up to a concentration of 20 per cent, showed any irritating effect on the cortex. Powdered sulfathiazole produced the same increased electrical discharge as the sodium salts. In the case of sulfapyridine powder the results were similar but less marked. Sulfadiazine powder produced no significant changes in the electrical activity. Therefore, the obvious conclusion is that sulfanilamide is by far the safest of the four sulfa drugs for the treatment of intracranial wounds in which the drug is likely to come in contact with the cortex.

ADRIEN VERBRUGGHEN, M.D.

SPINAL CORD AND ITS COVERINGS

Munro, D.: Cervical-Cord Injuries. *N. England J. M.*, 1943, 229: 919.

The author presents a series of 101 cases of spinal-cord injuries, situated in the canal of the cervical vertebrae. The mortality rate in this series of cases was 46 per cent. Forty-seven of the 55 survivals have been followed for periods of from six months to fifteen years.

Although bone changes or injuries are secondary to the cord damage, they must be recognized. In two-thirds of the cases of ascertained bone injury the fifth and sixth cervical vertebrae were involved. Of 44 cases with associated dislocations, 43 were anterior and only 1 was posterior. The recognition of dislocation by ligamentous tears without bone damage, in 11 cases, has convinced the author of the greater prevalence of cases in which realignment ensues before the patient is seen.

The most common pathological condition encountered was hematomyelia, with or without edema. Transection was done in 13 patients, with 2 survivals. Contusion resulted in great confusion, since no patient whose injury had been diagnosed as contusion was discharged with that diagnosis. Six other patients whose injuries were so diagnosed originally, had transections.

In the early stages of cervical-cord injuries, diagnosis is very difficult. Spinal shock will cause all reflexes to become chaotic. Testing for a spinal block is done by the fractional method with a blood-pressure cuff about the neck. The statement is made that "if a block is present, the patient is suffering from either edema, with or without hematomyelia, contusion, compression, or concussion of the cord. If a block is absent he is suffering from either hematomyelia without edema or an anatomical transection."

Nonoperative treatment consists of immediate treatment of the shock and the insertion of an indwelling catheter. A lumbar puncture always follows. The patient is placed on an ordinary hair mattress, and no special appliances, pads, or rings are allowed. A simple neck-halter extension with 5 lb. of weight is preferred to any other method of traction. The patient is turned every two hours by pulling the draw sheet tense, and while one person holds the head in proper alignment, others turn the tense sheet and thus carefully roll the patient into the desired position.

Fluid intake is maintained usually to about 4,000 cc. Some patients with paralytic extremities have developed pseudoarthritic changes which have been relieved by a high vitamin intake.

Roentgenography depends upon the spinal manometric findings and status of the patient. If no block is found, x-rays are relegated to a later date when the patient may be moved with greater ease. If a block is present, x-rays should be taken within seventy-two hours, if at all possible. Frequent x-ray checks are made from the time the patient is allowed up until complete healing has occurred. The patients are usually allowed out of bed with a modified Zimmer brace in from six to eight weeks. Careful scrutiny for possible redislocation must be maintained.

Operative interference is never performed until the effect of the injury has become stabilized, i.e., in about five to seven days. At that time, if still indicated, the decompression should be extensive enough to free the block completely. Manipulation of the bone structure is contraindicated since traction alone can do more, and with less trauma.

Transportation is a vital factor in the outcome of cervical-cord injuries. Patients should be carried in the face-down position, and before any change in body position is made the neck should be splinted.

JACK I. WOOLF, M.D.

SYMPATHETIC NERVES

Phemister, D. B., Laestar, C. H., Eichelberger, L., and Schachter, R. J.: Afferent Vasodepressor Nerve Impulses as a Cause of Shock: Tested Experimentally by Aortic-Depressor Nerve Stimulation. *Ann. Surg.*, 1944, 119: 26.

The most common theory as to the cause of so-called "primary shock" is that it is caused by excessive afferent depressor nerve impulses as a result of stimulations set up in the operative field or in the cerebrum. These in turn produce a stimulation of the vasomotor centers and, to a lesser extent, the cardiac centers in the medulla.

In an experimental study, shock could be produced by stimulation of (1) the trunks or receptors of the somatic nerves; (2) the proprioceptive aortic depressor and carotid sinus nerves; and (3) the cerebral depressor centers.

The present report deals with the method of stimulating the aortic depressor (cardioaortic) nerves in large rabbits. The animals were anesthetized with intraperitoneal urethane—500 mgm. per kgm. The nerve was exposed by a midline incision from the larynx to the sternum, while a kymographic recording of the blood pressure was obtained from the femoral artery.

In a control group of 3 animals in which the nerves were exposed in the routine manner, the average survival time was 14.66 hours. Hemodilution occurred in all animals but the blood pressure remained elevated until late in the experiment.

Continuous stimulation of the aortic depressor nerve maintained the blood pressure at shock levels for several hours without deleterious effects. On release of the stimulus the pressure promptly returned to within normal levels. Repetition of this at intervals revealed that the pressure tended to fall to lower normal and lower shock levels on release and reapplication of the stimulus, respectively. At longer periods, however, a decided hemodilution, anoxia, and damage to the vasomotor centers resulted in death. In 6 animals, the survival period averaged 6.75 hours.

To correlate the effect of hemorrhage upon a previous blood-pressure shock level, 11 animals were bled. If the bleeding was continuous the animal was killed by a smaller quantity of blood loss than one with intermittent bleeding. Although the latter was comparatively well tolerated, there was a reduction in the ability of the animal to withstand the blood loss. In other cases, lowered blood pressure was first obtained by bleeding in amounts of from 15 to 30 per cent of the estimated volume. Nerve stimulation after this resulted in a further drop of the blood pressure averaging 24 mm. of mercury, and a shortening of the survival time.

The effect of somatic afferent impulses on the blood pressure was studied by electrical (either tetanizing or slow make-and-break shocks) and mechanical stimulation of the saphenous and sciatic nerves. As has been shown in experimentations on other animals, only a momentary short rise or fall in the blood pressure ensued, which usually returned to normal, or at times remained slightly elevated. Thus, irritation of somatic nerves in an operative field is not a factor in the production of shock, except for manipulation in the upper abdomen, in which case the modus operandus is not known. The use of the term "primary shock" should be abandoned.

JACK I. WOOLF, M.D.

MISCELLANEOUS

Sal y Rosas, F.: The Relationship between the Onset of Experimental Convulsions and the Weight of the Patients (Relaciones entre el umbral de convulsion experimental y el peso de los sujetos). *Rev. neur.*, B. Air., 1943, 8: 3.

On the basis of 219 subjects (107 with a history of epilepsy and 97 without) the author discusses the data obtained from a study of the relationship between the onset of experimental convulsions and the weight of the individual. Cardiazol (pentamethylenetetrazol) was the drug used in bringing on the convulsions.

The first aspect of the problem led to a determination of the correlation between the minimum dose of the drug sufficient to bring on a convulsive seizure and the kilogram weight of the patient. It was found that considerable variation existed, the onset requiring anywhere from 1 to 6 cc. of the drug in patients weighing from 30 to 90 kgm. The groups contained epileptic and nonepileptic patients, and the epileptics were completely deprived of sedatives. In general, there appeared to be a direct relationship between the mean weight and the magnitude of the convulsive seizures. The nonepileptics, however, showed more consistency in their reactions than did the epileptics.

The mean dose-kilogram ratio for the epileptics was approximately 40 mgm. of the drug, and for the nonepileptics, 60.3 mgm. This ratio materially changed when the patient was under the influence of an anticonvulsive (barbiturate) drug. The dose-kilogram ratio was shown to be considerably elevated with the use of luminal.

STEPHEN A. ZIEMAN, M.D.

SURGERY OF THE THORAX

CHEST WALL AND BREAST

Haagensen, C. D., and Stout, A. P.: Carcinoma of the Breast. Criteria of Operability. *Ann. Surg.*, 1943, 118: 1032.

When edema involves a large area of skin over the breast, the dermal and subdermal lymphatics are extensively involved. This explains the clinical fact that patients with edema involving a considerable part of the skin over the breast are never cured by surgery. The authors classify patients with edema of more than one-third of the skin over the breast as categorically inoperable. Of 41 patients with such extensive edema, 65.0 per cent developed local recurrence in five years and none remained cured at the end of five years. In 12.5 of the cases in which the edema was limited to less than one-third of the skin of the breast, the patients remained clinically cured at the end of five years.

The authors define first-degree fixation of the tumor to the chest wall as the stage in which the tumor moves upward with the tensed pectoralis major muscle (the patient sitting upright), that is, it is fixed to the underlying pectoralis muscle only. Second-degree fixation is present when the tumor or breast is less passively movable when the pectoral muscles are tensed than when they are relaxed. This test is made with the patient in the prone position. Third-degree fixation is the stage in which the tumor is more or less solidly fixed to the chest wall even when the pectoral muscles are relaxed. Third-degree fixation is a grave sign, but the condition is not considered categorically inoperable. Fixed inframammary tumors do not have such a grave prognosis.

Satellite tumor nodules in the skin over the breast doubtless develop as the result of retrograde extension of the disease to the skin lymphatics. These are often not visible but may be palpated by passing the flat of the hand gently over the skin surface. Seven of 35 such cases were operated upon with no five-year cures (this group is categorically inoperable).

The presence of intercostal or parasternal nodules secondary to carcinoma of the breast are classified as categorically inoperable.

The presence of axillary lymph nodes over 2.5 cm. in transverse diameter suggests a grave prognosis. However, the authors advise a biopsy of the axillary glands of 2.5 cm. in transverse diameter, and if metastases are present the prognosis may be considered very grave; 20 per cent of the authors' cases had five-year cures. Likewise, if the axillary lymph nodes are fixed to the skin the prognosis is poor, there having been 1 five-year cure among 7 cases.

Edema of the arm is evidence of extensive axillary lymphatic involvement and is classed as categorically inoperable, as is supraclavicular lymphatic involvement. Likewise, inflammatory carcinoma of the breast is placed in the same inoperable group.

The authors believe that distant metastases offer such a grave prognosis (and radical mastectomy may shorten the patient's life) that they carefully inquire and examine for such metastases. They inquire about any recent development of headache, pain in the back of the legs, a recent cough or pain in the chest; and they carefully run the hand over the skin of the chest and back, palpate the opposite axilla, and the liver. They make a roentgen-ray examination of the chest, and of the entire skeleton with exception of the forearms and hands, the lower legs and feet. Even in the absence of x-ray evidence of metastases to the bones a suggestive history is not ignored.

Also, carcinoma developing during pregnancy and lactation is considered categorically inoperable.

If two or more of the following signs of locally advanced carcinoma are present the authors classify the case as inoperable:

1. Ulceration of the skin
2. Edema of the skin limited to less than one-third of the skin of the breast involved
3. Fixation of the tumor to the chest wall
4. Axillary lymph nodes 2.5 cm. or more in transverse diameter, and proved to contain metastases by biopsy
5. Fixation of axillary lymph nodes to the skin or deep structures of the axilla, and proved to contain metastases by biopsy.

EARL O. LATIMER, M.D.

TRACHEA, LUNGS, AND PLEURA

Schmidt, H. W.: Benign Nontuberculous Bronchial Stenosis. *Arch. Otolar.*, Chic., 1944, 39: 43.

Benign nontuberculous bronchial stenosis is a rather common complication of respiratory infection but it is rarely recognized. It is important that more study be given to this type of lesion so that diagnostic accuracy may be increased and proper treatment instituted.

An antecedent respiratory infection, such as pneumonia, severe tracheobronchitis, or asthmatic bronchitis, can cause bronchial obstruction. After stenosis has occurred it produces a rather typical clinical picture which is characterized by recurrent chills and fever, cough, purulent secretion, and general malaise. The physical and roentgenographic findings vary. They sometimes indicate partial atelectasis of a lower lobe of one lung. In other cases they may be negative. Bronchoscopy is the only accurate method of diagnosing such a lesion.

This article is based on a study of 25 cases of benign nontuberculous bronchial stenosis in which bronchoscopy was performed by the author. Four of these cases are reported in detail.

Analysis of the results of treatment was based on the 19 cases in which follow-up data were available. In most of these cases bronchoscopy was performed

from three to six years before this report was made. Four patients obtained complete relief of symptoms; 6 patients obtained marked relief which has persisted up to the present time; 3 patients obtained marked relief but had a recurrence of symptoms twenty-four, twenty-five, and thirty-six months, respectively, after bronchoscopy; 1 patient obtained moderate relief for two and one-half years and then had a recurrence of symptoms; 1 patient has had moderate relief for three years and three months; and 1 patient obtained relief for four months and then had a recurrence of symptoms. In the remaining 3 cases the patients apparently were not benefited by the treatment.

Chesterman, J. T.: Evaluation and Treatment of Factors Involved in Postlobectomy Collapse of the Lung. *Arch. Surg.*, 1943, 47: 448.

The status of pulmonary resection for suppurative disease has improved remarkably in the last decade. This is shown in the lowering of the mortality rate from 50 per cent to an average of 10 per cent, and in some clinics it is as low as 2½ per cent. The problem at the present time is to prevent postoperative collapse of the lung and to maintain maximum postoperative function.

Three main types of collapse of the lung following lobectomy are recognized:

1. The complete form which prevents circulation of air while maintaining circulation of the blood. This form is due to an elastic recoil of the lung. As the air is absorbed by the blood stream further loss of aeration may be produced by obstruction of the air passages, either extrinsic or intrinsic.

2. The second and more common form is the result of a lack of expansion of the remaining lung tissue to fill the thoracic cavity, due to fibrosis following inflammation of the lungs.

3. The third type has been mentioned by various authors and is due to reflex action. However, the author questions this type.

In the production of postlobectomy collapse, bronchial obstruction and fibrosis (the latter due to operative trauma or infection) are the most important factors. Pressure from encysted fluid may be significant.

Prior to operation the use of iodized oil may play a significant role in the postoperative condition of the lung. In 25 cats, 5 cc. of iodized oil were injected. Three of the group had a second injection and 1 had three injections. Lipid pneumonia occurred in 3 of the 25 cats. The first had only one injection and died of anoxia four weeks after lobectomy. The second cat had 2 injections and nine days following the second dose was found moribund. Large areas of collapse due to lipid pneumonia were present. The third had the first injection a month before operation and a second injection two weeks following. It died of diffuse lipid pneumonia two weeks later.

In a review of 50 patients who had received iodized oil, no relation was found between the time of administration, the number of administrations, the quantity of oil used, and the amount of oil still present in the lungs at the time of operation.

In another series of 51 cases only 2 developed a collapsed lobe on the side opposite from that of operation.

In an attempt to prevent collapse by the formation of adhesions, considerable attention has been given to the fusion of the two pleurae prior to operation. The most reliable method of producing this has been the insufflation of the pleural cavity with talc powder containing 0.5 per cent iodine. This procedure was carried out in 22 cats. In 7 of these a lower lobectomy was done fourteen days later. Three presented some adhesions about the upper lobe, the lower lobe being practically free. Two showed marked mediastinal adhesions of both lobes. One presented adhesions only about the basal lobe and one had lesions in both the basal and apical portions.

Thus it is seen that adhesions cannot be accurately controlled and cannot prevent the two common forms of collapse from occurring. Also, adhesions have been shown to cause postlobectomy collapse. For these reasons the author believes that the artificial production of adhesions should be abandoned and adhesions found at operation should be sectioned if they are likely to give rise to distortion of the remaining lung tissue.

Following lobectomy in patients, continuous suction should be maintained by a tube leading from the pleural cavity and connected with a negative pressure apparatus. This will tend to remove secretions and encourage expansion of the remaining lung. Cough is encouraged and manual support should be given the patient's wound when an effective cough is prevented by pain.

WILLIAM E. ADAMS, M.D.

Price, H. J.: The Relief of Acute Pleuritic Pain by Intercostal Nerve Block. *J. Am. M. Ass.*, 1943, 123: 628.

The author reports 14 consecutive cases of severe pleural pain relieved by intercostal nerve block. Procaine hydrochloride is injected into the groove occupied by the intercostal nerve and vessels after ascertaining that the needle has not entered a vessel. The groove of the rib, above the intercostal space over which tenderness is elicited by pressure, is injected.

Thirteen patients who had pneumonia and a fourteenth who had pulmonary infarction were suffering with severe lancinating pleural pain aggravated by cough and deep inspiration. All but 3 of those with pneumonia had audible friction rubs. The pain recurred in only 2 patients but reinjection of the nerves produced permanent and complete relief of the pain.

The author believes that the permanent relief of pain might be due in some way to the increase in depth of respiration and the increased motion of the parietal pleura.

FREDERIC W. ILFELD, M.D.

HEART AND PERICARDIUM

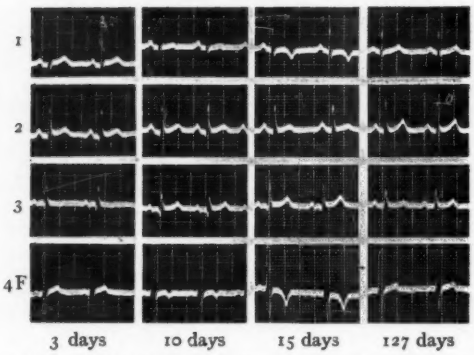


Fig. 1. Serial electrocardiograms following a blow over the precordium of a healthy young man. Deep late inversion of T in Leads 1 and 4F is seen to reach a maximum at fifteen days, with later return to normal configuration.

Lee, R. V., Ussher, N. T., and Houck, G. H.: Acute Traumatic Heart Disease. A Case of Myocardial Contusion with Recovery. *Am. J. M. Sc.*, 1943, 206: 722.

A case of acute traumatic heart disease is reported. There was little likelihood of pre-existing heart disease.

The patient was observed early, and an essentially normal electrocardiogram was obtained at the onset of the disease. The symptoms, clinical course, and the series of tracings, which revealed serial changes, were pathognomonic of myocardial injury. This may have been merely a cardiac muscle contusion, or, as seems less likely to the authors, the contusion may have progressed to a myocardial infarction. There is little reason to believe that any degree of coronary-artery occlusion occurred.

CHARLES BARON, M.D.

Nelson, H.: Penetrating Wounds of the Heart: A Routine of Management Based on a Five-Year Period of Personal Observation and on 5 Personal Cases. *Arch. Surg.*, 1943, 47: 571.

The classic picture of cardiac wounds includes: (1) a period of freedom from symptoms, followed by rapid collapse and unconsciousness; (2) weak heart sounds associated with a weak pulse; (3) lowered arterial pressure, and (4) elevated venous pressure. However, it is to be emphasized that this picture is not present in all cases. A wound of the heart is a possibility in any instance of penetrating thoracic injury, particularly when there is eivdence of (1) cardiac tamponade, (2) progressive tension pneumothorax, (3) marked or progressive hemothorax, and (4) shock other than that resulting purely from traumatic stimuli.

The author describes the illogic of conservative therapy for cardiac trauma, the routine of management, the anesthesia, and the surgical technique, as well as the postoperative therapy. An analysis of cases is included. He believes that in recent years the number of operations for wounds of the heart has increased, and the mortality has decreased. Conservative therapy of cardiac wounds has given poor results, and the author believes that such wounds should be treated as any other wounds in which hemorrhage is a factor.

The most important reason for the reduction in the mortality in cases of penetrating wounds of the heart is the policy of performing an exploratory operation in all cases of penetrating thoracic wounds in which it cannot be determined positively that the wound has not reached the heart.

EMIL C. ROBITSHEK, M.D.

Jorge, J. M., and Re, P. M.: Hydatidiform Cysts of the Heart (Hidatidosis cardiaca). *Rev. As. méd. argent.*, 1943, 57: 720.

A primary hydatidiform cyst of the myocardium may develop from an infestation carried from the lymphatic paths through the subclavian vein into the heart. The presence of hydatidiform cysts in the heart without a concomitant location in the liver or lungs points to a hematogenous-transendocardiac route of the infection, without the hematogenous-coronary route which would require that the bacteria pass through the pulmonary capillary filter.

Systolic contractions of the heart muscle may be transmitted to the cysts located within the myocardium, with the resulting expulsion of its metabolic products which may produce a desensitization or immunization of the organism. This hypothetical mechanism explains the frequent absence of symptoms due to a solitary cyst.

A differentiation may be made between (1) primary cardiac hydatidosis which is produced by the entry of ova of the echinococcus tenia into the organism, their transformation into embryos in the digestive tract and passage through the intestinal wall, and penetration of the myocardium by the larvae, and (2) secondary cardiac hydatidosis in which the scolex reaches the heart from other organs.

The ventricular location of the cysts predominates over the auricular location. The location on the left side is more frequent than on the right, but ruptures occur more frequently on the right side.

JOSEPH K. NARAT, M.D.

ESOPHAGUS AND MEDIASTINUM

Poth, E. J.: Congenital Atresia of the Esophagus. *Surgery*, 1943, 14: 882.

Congenital atresia of the esophagus occurs sufficiently infrequently that few physicians see many of these anomalies. The surgical treatment of this condition has been most unsatisfactory, but it appears now that the solution of this problem is not far distant. It seems desirable, therefore, that any possible attack on this problem be reported so that the technique may be incorporated into whatever pro-

cedure may soon prove itself. An operation is described for the treatment of the commonest type of this lesion (the upper end of the esophagus being blind and the lower segment communicative with the trachea), which promises some success.

After the insertion of a No. 14 French soft rubber catheter into the upper segment of the esophagus, the patient is placed in the prone position with the right arm extended over the head. Because of the danger of inadvertently opening the pleura with collapse of the lung, provision must be made to administer the anesthetic under pressure. During the previous fluoroscopic examination a paper clip is fixed over the right fifth rib posteriorly under a strip of adhesive. When the skin is prepared, the metal clip is removed, and its impression on the skin marks the level of the fifth rib accurately. The incision begins at the level of the second rib, extends downward just to the right of the midline to the level of the fifth rib, to turn laterally along the lower border of the scapula, and is carried outward to the posterior axillary line. Two inches of the fourth rib are excised subposteriorly, the excision extending outward from the transverse process. The third and fifth, and occasionally the second and sixth, ribs are transected close to the transverse processes. The pleura is exposed by a T-shaped incision extending outward just superior to the fourth rib and including the section of the third, fourth, and fifth intercostal muscle bundles, nerves, and blood vessels as near the transverse processes as possible. The operator enters the mediastinum by staying close to the vertebral column and carefully pushing aside the pleura. The horizontal portion of the azygos vein, where it crosses above the bifurcation of the trachea to join the superior vena cava, is the first prominent structure encountered. This vessel should be divided to give a direct approach to the esophagus at a level just superior to the carina. Careful dissection of the immediate areolar tissue will uncover the esophagus. If at this point the anesthetist will push on the catheter, its tip is readily identified, provided the upper segment is sufficiently long to allow anastomosis between the two segments of esophagus. The presence of the catheter likewise shows the anteroposterior level of the esophagus and gives an excellent guide to its lower segment. A small electric bulb on a flexible carrier, passed into the catheter, is an additional aid in locating the tip of the catheter even though the upper segment is too high to permit anastomosis of the segment. The upper and lower segments of the esophagus cannot be anastomosed if the ends are separated by more than 2 cm. without extensive freeing of the distal segment. The tracheoesophageal fistula is identified, isolated, and ligated adjacent to the trachea. If an immediate anastomosis is possible, the distal segment of the esophagus is divided, as near the tracheoesophageal fistula as possible. If, however, an anastomosis is impossible, the esophagus is doubly ligated and divided between the ligatures, and the first-stage operation is complete.

For immediate anastomosis, minimum lengths of the upper and lower segments of the esophagus are freed. The end of the upper segment is fixed with a traction suture and opened, the catheter is directed into the lower segment and pushed down to enter the stomach, and the esophagus is anastomosed over the catheter, by means of 4 simple interrupted sutures.

After it has been determined that the pleura has not been accidentally damaged and that air has not entered the pleural space, the wound is lightly powdered with sterile sulfanilamide and closed. A simple rubber tissue drain extends into the depths of the wound.

With a tube in the stomach, the infant can be fed immediately and should be given its formula in small amounts each hour. The tube is left open between feedings. The patient is turned frequently and the head is kept lowered and turned to one side. Sulfadiazine should be given before operation and this therapy should be continued postoperatively as a safeguard against pneumonia. J. M. Mora, M.D.

SURGERY OF THE ABDOMEN

GASTROINTESTINAL TRACT

Johnstone, A. S.: Peptic Ulceration of the Esophagus with Partial Thoracic Stomach. *Brit. J. Radiol.*, 1943, 16: 357.

Seven patients with peptic ulcer of the esophagus have been encountered by the author. All patients had marked shortening of the esophagus with a small hiatus hernia and partial thoracic stomach.

Since these lesions are encountered in elderly people, particularly in those of sthenic build, the hiatus hernia is believed in many instances to be acquired, and to be the result of senile changes in the tissues forming the hiatus rather than the result of a congenitally short esophagus, although the latter type undeniably occurs.

The diagnosis of hiatus hernia was made by roentgenological methods which demonstrate a change from esophageal to gastric mucosa. In the author's cases of peptic ulcer of the esophagus, there was widening of the upper esophagus and a moderately abrupt tapering to an area of stenosis from 6 to 12 cm. above the diaphragm, which terminated in a wide channel and was easily recognized as stomach when filled with barium. The ulcer crater usually was shallow and impossible to differentiate from an irregularity due to spasm or fibrosis. Occasionally it was well defined.

The genesis of peptic ulceration in the esophagus is believed to rest in the frequent regurgitation of acid in conjunction with other factors, such as laxity of the cardia and hiatus, vomiting, and the existence of an ulcer diathesis. The peptic ulceration, in turn, becoming chronic, may produce enough scarring to shorten the esophagus and produce a partially thoracic stomach.

EDWARD W. GIBBS, M.D.

McSwain, B., and Beal, J. M.: Lymphosarcoma of the Gastrointestinal Tract. *Ann. Surg.*, 1944, 119: 108.

Twenty cases of lymphosarcoma of the gastrointestinal tract, confirmed by microscopic examination, have been treated in the New York Hospital during the past nine years. They represent 1.9 per cent of all cases of malignant lesions of the gastrointestinal tract at this hospital.

Lymphosarcoma may be found in any part of the gastrointestinal tract. In 1 case the lesion was in the esophagus; in 7 cases the lesions were in the stomach; in 3, in the small intestine; in 2, in the appendix; and in another 7, in the large intestine, including the rectum. No lesions were noted in the duodenum in any of the cases.

In this series there were 13 males and 7 females whose ages ranged from four and one-half to seventy-one years; the average age was forty-three and two-tenths years.

The clinical manifestations, and the laboratory, roentgenological, and operative findings are reviewed. The correct diagnosis is seldom made preoperatively. In this series the preoperative diagnoses were as follows: lymphosarcoma in 3 cases, carcinoma in 10 cases, intussusception in 2 cases, appendicitis in 1 case, and left ovarian tumor in 1 case. Three cases of lymphosarcoma of the rectum were diagnosed preoperatively as rectal polyps or fissure-in-ano.

Thirteen of the 20 patients received x-ray therapy. Two of these did not tolerate it and both died of fulminating lymphosarcoma before the outlined dosage could be given.

The survival of the patient is influenced more by the site and extent of the growth than by his age or the histological structure of the lesion. In 6 patients the neoplasm was well localized and apparently without lymph-node involvement. In all of these the lesion was excised and x-ray therapy was not given. None of these patients has shown evidence of metastases from two to seven years after operation.

Six patients received x-ray therapy alone. Only 2 of these are free of recurrence.

In 6 cases resection of the lesion was followed by x-ray therapy. Only 2 of these are free of recurrence.

Nine patients are alive and well without evidence of recurrence from one year to nine years and five months after the diagnosis was established. Eight patients have died, and the average duration of life in this group after establishment of the diagnosis was two years.

The best prognosis is found in the cases suitable for complete excision of the lesion. X-ray therapy should be given to every patient with lymphosarcoma of the gastrointestinal tract unless the operator and the surgical pathologist are certain that the lesion has been completely excised.

EDWARD W. GIBBS, M.D.

McCabe, E. J., and Mersheimer, W. L.: Acute Gastroduodenal Perforations. Review of Metropolitan Hospital Series 1930. *Am. J. Surg.*, 1943, 62: 39.

The authors review the subject of perforated peptic ulcers as well as the etiological factors involved, the symptoms and diagnosis, and the operative procedures. A series of 89 consecutive and unselected cases are presented from the Metropolitan Hospital, New York, from 1930 to 1941, inclusive.

The diagnosis of ruptured gastroduodenal ulcer should be made without great difficulty in nearly every case. Close questioning of the patient will elicit a history suggestive of or definite of ulcer in 75 per cent of the cases. The sudden onset of the present illness and the severity of the pain with rapid spread throughout the abdomen, and perhaps to one or both shoulders, will frequently lead one to suspect the diagnosis. The physical signs that are outstanding

are the boardlike rigidity of the abdomen and the "silent" abdomen on auscultation. Diminution of liver dullness and roentgenographic evidence of pneumoperitoneum are pathognomonic for a ruptured viscus. Ingestion of a dye solution by mouth and recovery by peritoneal aspiration is pathognomonic of ruptured gastrointestinal tract. When a diagnosis of perforated viscus cannot be confirmed by the pathognomonic features mentioned, determination of the serum amylase should be made to exclude the possibility of acute pancreatitis.

When laparotomy is decided upon the patient should be given intravenous fluids preoperatively, if necessary, to combat shock or dehydration. Morphine should be freely employed. An empty stomach should be insured by preoperative use of the nasogastric tube and Wangensteen suction, which should be continued through the operation and postoperative phase. Spinal anesthesia facilitates the operation. A small high incision should be employed and simple plication with reinforcement with omentum should be the only procedure in the majority of cases.

If the patient is an exceptionally good operative risk, if the perforation has been present less than six hours, if the degree of peritonitis is not advanced, and if the operator has considerable experience at gastric resection, primary subtotal gastric resection should be considered. When the perforation has been present more than six hours, the intraperitoneal application of sulfonamides is mandatory. Extreme care must be used in closing the incision. Retention sutures should be employed and steel-alloy sutures can be used advantageously. Postoperative care should emphasize the prevention of gastric dilatation by continuous gastric suction; prevention of anoxia by routine administration of oxygen, preferably by means of masks during the critical postoperative period; intelligent administration of fluids (whole blood, plasma, or glucose and saline); and early recognition and treatment of hypoproteinemia and vitamin deficiencies. CHARLES BARON, M.D.

Raw, S. C.: Perforation of Gastric and Duodenal Ulcers. *Lancet*, Lond., 1944, 246: 12.

The author reports his experience and results in a large series of perforations of gastric and duodenal ulcers.

During the five years from 1937 to 1941, the perforation cases admitted to the Royal Victoria Infirmary showed a steady rise, as follows: 181, 198, 200, 232, and 251, a total of 1,052. The average age of the patients was about forty-two years. In the vast majority of cases the patient was a man and the ulcer was situated in the duodenum. In a diagnosis of atypical cases, the following conditions must be ruled out: coronary thrombosis, pleurisy, cholecystitis, pancreatitis, perforated appendicitis, renal colic, and obstruction of the small bowel.

In perforations the onset of symptoms is nearly always dramatic, with little vomiting or change in pulse and temperature. The pain does not vary and the patient usually lies still. Breathing is short and thoracic in type. In pleurisy, rigidity may sometimes be overcome by holding the breath; in colic it is usually overcome by breathing; but in perforations it never leaves completely.

Before operation at least 60 per cent of the patients have pain referred to one or both supraclavicular regions, due to irritation of the undersurface of the diaphragm by gastric contents or bile. The author considers diminished liver dullness a dangerous and misleading clinical sign. It is present only in obvious cases and one must take account of variations in the normal size of the liver, paralytic distention, intestinal obstruction, and emphysema of the lungs. Roentgenography sometimes shows free gas beneath the diaphragm. When this picture is taken an anteroposterior film with the patient lying on the left side may be particularly useful. The pulse and temperature remain normal a few hours only and are of little help in differentiating a twenty-four-hour perforation from any other peritonitis, provided the temperature is under 101° F. In such a case reliance must be placed on a careful history of the onset, early pains in the tip of the shoulder, or persistent rigidity of the upper right rectus muscle. A combination of upper and lower abdominal rigidity usually indicates a primary upper abdominal peritonitis.

Morphine should be given at once. One or two pints of blood plasma should be given in severe shock.

If the pulse rate is over 100 per minute and the systolic pressure under 100 mm. of mercury, the patient should be regarded as seriously ill. In most cases of early perforation open anesthesia was found satisfactory. This was greatly facilitated by injection of the rectus sheath with 1 per cent procaine. Local anesthesia is the author's choice in severe cases; injections are given beneath the costal margin, deep to the external oblique muscle, in the line of the skin incision. If the perforation is a little inaccessible and it is found necessary to pull on the mesenteries, additional intravenous use of pentothal is advisable. This also facilitates aspiration or the mopping of fluid from the subphrenic spaces. The author considers spinal anesthesia to be contraindicated when subphrenic irritation exists.

A nasal catheter is used to keep the stomach empty. Five per cent glucose and saline solution injected in the axillary region, or intravenously if indicated, is routine in the author's cases.

Among the complications are general peritonitis and pelvic abscess; lung, liver, and brain abscesses are nearly always fatal; subhepatic, subdiaphragmatic abscesses and empyema thoracis are found satisfactory for treatment if recognized early. The recollection of Rutherford Morrison's aphorism — pus somewhere, pus found nowhere—therefore subphrenic abscess — is often lifesaving. Most cases of subphrenic abscess following perforation are on the right side, beneath the diaphragm and between the duodenum and the liver. These can be drained through a subcostal incision under local anesthesia. This incision, though not the most direct, avoids the risk of empyema.

TABLE I.—SITES OF PERFORATION IN 312 CASES

	In Males	In Females	Total
Gastric	11	4	15
Pyloric	8	1	9
Duodenal	269	13	282
Anastomatic	5	1	6

TABLE II.—RELATION OF MORTALITY TO AGE

Under 42 years .....12 deaths in 157 cases (7.6%)
Over 42 years .....33 deaths in 155 cases (21.3%)

Perforated ulcer is an important abdominal disease. The patients are usually in the prime of life. The mortality rate varies greatly with early diagnosis, experience, and careful surgery. In wartime considerable preoperative malnutrition and vitamin deficiencies often act as formidable complications. Stormy convalescence often is caused by dehydration, massive collapse of the lung, and subphrenic abscess. Careful postoperative observation and nursing often prevent, or at least lead to the detection of, such complications early enough for successful intervention. "The fatality-rate runs closely parallel to the number of hours between perforation and operation."

Advancing years make the prognosis worse.

Perforations are uncommon in women but are a trap for the unwary. Sedatives given for erroneous diagnoses, as gallstones, etc., delayed correct treatment in over half of the author's cases for more than eighteen hours, and caused a shocking mortality rate.

Operative intervention should be minimal, reasonably rapid, and gentle. MATHIAS J. SEIFERT, M.D.

Spicer, C. C., Stewart, D. N., and Winser, D. M. de R.: Perforated Peptic Ulcer during the Period of Heavy Air-Raids. *Lancet*, Lond., 1944, 246: 14.

The heavy air raids in London caused a rise in the incidence of perforated peptic ulcers. The figures from 16 London hospitals confirm that this rise was no mere artifact. This is best demonstrated by the following statistics giving the average number of perforations per month for successive periods from 1937 to 1942. The heavy air-raid period was considered to extend from September, 1940 to May, 1941, inclusive.

	No. of occurrences per month
January to September, 1937	21.8 %
October, 1937 to June, 1938	22 %
July, 1938 to March, 1939	25.9 %
April to December, 1939	25.5 %
January to August, 1940	22.4 %
September, 1940 to May, 1941 (Blitz period)	35.11%
June, 1941 to February, 1942	20.3 %
March to November, 1942	16.5 %

The above figures show that there is considerable evidence that anxiety might be an important cause of peptic ulcer. Especially during the Blitz period some new general cause was operating.

The authors, in a previous article, summarized the available evidence on the causation of peptic ulcer and its complications and stressed anxiety as supposedly an important cause.

SUMMARY

The increase in perforated peptic ulcer during the period of heavy raiding was statistically significant when compared with the incidence of the previous three, and the following two years.

There is statistical evidence of a tendency toward perforation during the air-raid period and of a similar tendency during the two following years.

There was also a significant increase in perforations during the month of December.

MATHIAS J. SEIFERT, M.D.

Feldman, M.: The Life Cycle of Carcinoma of the Stomach. *Gastroenterology*, 1944, 2: 60.

Three cases are presented which portray an interesting picture of the life cycle of carcinoma of the stomach. Repeated roentgen examinations were made in each case over a number of years, which enabled the author to study the sequence and progress of the growth from the onset to the final stage. The cases presented the clinical picture of peptic ulceration with periods of remissions.

These cases had similar roentgen findings of narrowing of the prepylorus, involvement of both curvatures, and fixation of the curvatures with a plateau appearance of the lesser curvature in the affected area. The carcinomas were slow-growing, as they had existed for many years. Two of the patients had persistent low gastric acidity, while 1 showed a persistent hyperacidity throughout the entire course of his illness. In all 3 cases the patient finally developed a pyloric obstruction because of an inoperable carcinoma.

The author remarks that negative roentgenological information regarding the integrity of the stomach often gives one a sense of false security. The demonstration of a narrowing of the pylorus should lead one to suspect a possible lesion. If a patient with a digestive disorder presents a negative gastrointestinal study but is clinically getting progressively worse or is not improving, an organic lesion somewhere in the gastrointestinal tract should be suspected, and repeated roentgen studies should be made at intervals. JOSEPH K. NARAT, M.D.

Berk, J. E., and Dunlap, H. J.: Hypertrophic Pyloric Stenosis in Adults. *Ann. Surg.*, 1944, 119: 124.

The authors report 2 cases of simple hypertrophic pyloric stenosis in adults. Both patients were in the fourth decade of life, both were in the Army, and both presented a comparatively brief ulcerlike history associated with symptoms and signs of partial and complete pyloric obstruction. At operation both patients had a pyloric mass, the exact nature of which was uncertain, and as the possibility of malignancy could not be excluded at operation, the mass was removed in both cases by subtotal gastric resection.

Gastroscopic examination prior to operation had revealed no mucosal abnormalities in either case. However, chronic gastritis was demonstrated by histological study of the resected stomachs. The exact relation between the chronic gastritis and the muscle thickening was obscure.

EDWARD W. GIBBS, M.D.

Noble, T. B., Jr.: Perforating Wounds of the Intestine; Satisfactory Method of Treatment for Wounds More than Twenty-Four Hours Old. *Am. J. Surg.*, 1943, 62: 50.

Unless certain pathological sequences are understood, failure attends any method of treating perforating gunshot wounds of the intestine. Peritonitis is not often to be feared because of its infectious toxicity; it is the obstructive element always produced by the early, rapid processes of localization or repair that kills. Surgery, therefore, must control all tendency toward obstruction resulting from injury or inflammation. The method of plicating the gut as illustrated has proved to be adequate in some hundreds of cases of all degrees.

In Figure 1 the simplest unit of plication is shown. To cover a damaged mesenteric or intestinal peritoneum of the small bowel, plication is done in single wing. To repeat, a running suture of any material, begun at point A, is continued on, bringing lines AC and AD together to form line A-CD, then continued as desired to cover the area to point B, at the wing apex. Figure 2 shows a three-wing plication which will cover raw areas on four surfaces of the mesentery and intestine. The lettering is arranged to show juxtaposition of single units of plication. Figure 3 demonstrates the application of single units varying in size as desired and placed adjacent to each other so that the effect is a continuous plication. In each unit the suture is always started at the root of the mesenteric fold, and is tightly closed. The entire

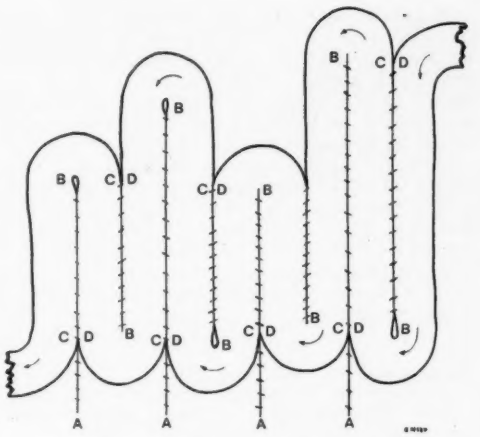


Fig. 3. Continuous plication (Courtesy of Am. J. Surg.).

small bowel may be plicated, and it is safer to plicate completely than to miss covering one raw area.

Additional supportive measures after surgery, such as blood transfusion and plasma infusion, are as much a part of the care of the case of advanced peritonitis, as are food, drink, and rest of normal life.

Spinal anesthesia is preferred because active peristalsis is wanted as soon as possible to follow the surgical efforts. Immediately after surgery, pituitrin (no other substance is as free from disadvantages) is given hourly until the abdomen is empty and fluid stools are obtained with each injection. Then feeding is begun along the same lines followed in clean surgery. After complete plication, obstructive signs cease and convalescence is very rapid, even though a

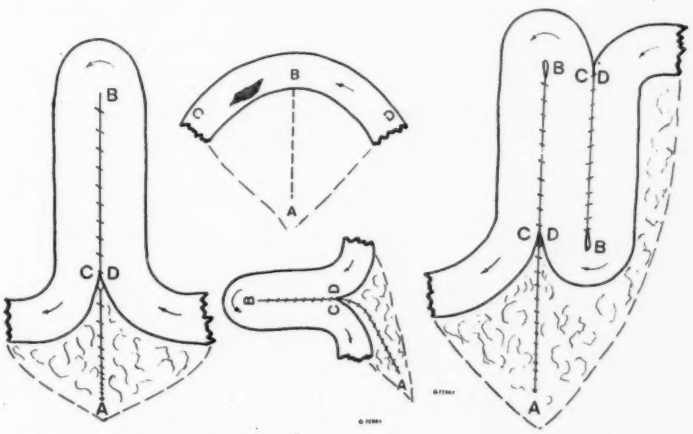


Fig. 1. Left, The simplest unit of plication. Fig. 2. A 3-wing plication.

hard rubber drain into the bottom of the pelvis shows much pus of the colon type to be forming over a period of time after operation. Since abscesses are multiple in number, type, and size in any case, a drain is always left down to the bottom of the pelvis and brought out through a stab wound so that there will be no fluid accumulation about the pelvic colon.

In view of our present rather definite and accurate knowledge of the pathological sequences of peritonitis and their effects, a method of therapy has been applied to them which has prevented the unhappy outcome that is known to follow the existence of intestinal perforations for more than twenty-four hours. This method has given better than 90 per cent recovery in place of the former 90 per cent fatality.

CHARLES BARON, M.D.

Winkelstein, A., and Levy, M. H.: Lymphosarcoma of the Intestines: 15 Cases; Characteristic Sigmoidoscopic Picture. *Gastroenterology*, 1943, 1: 1093.

Lymphosarcoma of the intestines is a rare disease of unknown etiology. The tumors arise from the lymph nodes and lymph follicles of the submucosa. They increase in size, obliterate the structure of the glands and follicles, and, unlike the leucemic tumors, grow beyond the capsule of the gland. The submucosa and muscularis are invaded and a subserosal tumor is formed. A chronic peritonitis with adhesions results. The growth may either (1) remain as a localized polypoid mass extending into and partially obstructing the lumen of the bowel, or (2) it may spread out longitudinally and (a) cause a diffuse thickening of the bowel wall, or (b) produce an aneurysmal dilatation through central ulceration and necrosis with excavation of the growth. This aneurysmal dilatation may also be due to the weakness of the musculature resulting from invasion. Lymphosarcoma of the small intestine usually results in aneurysmal dilatation of the affected loop, rarely in a stenotic lesion. In the rectal cases, however, stenosis is more common. The mesenteric lymph nodes are involved early in the disease. This is a consistent finding at operation or autopsy. Metastases to distant organs, especially the kidneys, liver, and spleen, may occur. Lymphosarcoma of the intestines rarely causes perforation of the bowel. In the small intestine, intussusception is not uncommon. In the rectal cases, a varying degree of obstruction is frequent. Massive hemorrhages are rare. The small intestine is more often affected than the large bowel. Multiple intestinal lesions are not uncommon. While the average age incidence is 43.7 years, it may occur at any age.

The histological differentiation into small-cell lymphosarcoma and reticulum-cell sarcoma is unimportant clinically.

The onset of the symptoms of lymphosarcoma of the intestine may be acute or insidious. An acute beginning may simulate an acute surgical condition of the abdomen, especially appendicitis. It is more common, however, for the disease to make its appearance gradually. Distention of the abdomen is a frequent symptom. It appears early in the course of the disease and often is the first cause of complaint. Pain is usually present; it may be localized in the involved part of the abdomen or it may be generalized throughout the abdomen; the pain is of a colicky type, rather constant, and unaffected by food. The pain of lymphosarcoma of the intestines is generally not very severe. In many cases a mass is palpable in the abdomen. The mass is usually slightly tender and rarely very painful; as a rule, it is freely movable. Anorexia, weakness, and marked emaciation are present in the majority of the cases. These general symptoms are usually early manifestations of lymphosarcoma and often precede the abdominal symptoms. A change in bowel habit is rather characteristic of the disease. An evening rise of temperature to 101 or 102 degrees is not rare. Quite striking is the absence of severe anemia.

There are no absolutely characteristic x-ray findings in lymphosarcoma of the intestines, but there is frequently a characteristic, practically diagnostic sigmoidoscopic picture which resembles the surface of the brain.

The outlook is poor. The treatment of lymphosarcoma of the intestines consists in radical removal of the tumor combined with radiotherapy. Only in those cases in which surgery is impractical should x-ray and radium treatment be used alone.

Among the 15 cases observed at the Mount Sinai Hospital in New York from 1932 to 1942, 11 of the patients were males. Nine patients were between the ages of twenty-nine and forty-one years, and 6 between the ages of fifty-two and sixty-five years. There were no children in this series.

JOSEPH K. NARAT, M.D.

Warren, H. A., and Emery, E. S.: Duodenal Diverticula. *Gastroenterology*, 1943, 1: 1085.

A perplexing problem arises whenever duodenal diverticula are found in a roentgenological report, since it must be decided whether or not the lesions are the cause of the patient's symptoms. According to the literature, which the authors have carefully reviewed, there are no characteristic diverticular symptoms. Many diverticula give no symptoms and would go unnoticed without the aid of x-rays.

In a study of 103 cases of duodenal diverticula the authors attempted to determine what, if any, symptom-pattern existed with the lesion. They found that no typical symptomatology could be established. The 103 cases studied were found in the records of the Peter Bent Brigham Hospital, Boston, Massachusetts, from 1914 to 1941. This represents an incidence of 2.3 per cent of the cases showing roentgen evidence of gastrointestinal disease. The average age of patients with duodenal diverticula is fifty-eight years. The findings showed 39 of the patients to be males and 64, females, which is a reversal of the usual findings in which the males predominate. The size of the duodenal diverticula varied from ½ to 6 cm., as measured on the x-ray film.

The location of a diverticulum and its relation to neighboring structures may be important. The authors found that in 8.7 per cent of their cases the lesion occurred in the first portion of the duodenum; in 65 per cent, in the second part; and in 15.5 per cent, in the third part. In 6.8 per cent of their cases multiple diverticula of the duodenum occurred. A careful study of these cases showed that the diverticula found in the first portion of the duodenum were usually of the false type, since all of the intestinal layers were intact, and that they appeared to be associated, in most instances, with duodenal ulceration. The diverticula found in the second portion of the duodenum were usually true herniations of the mucosa through the muscular wall. Not infrequently, a fair number of these showed inclusions of the pancreatic tissue. The cases of diverticula arising from the third portion of the duodenum were fewer in number. All of the lesions were in close proximity to the pancreas. One of them showed a localized abscess.

The authors state that it is difficult to make an entirely satisfactory evaluation of the role which the diverticulum may have played in these cases. It is fair to say that no characteristic group of symptoms emerged from this study. The described symptoms of the patients who were found to have either organic disease, like ulcer or gall-bladder disease, or a functional disorder such as mucous colitis and constipation, were such as could be explained by these other findings.

From this study it appears definite that there is no syndrome characteristic for duodenal diverticula. However, it is impossible to conclude absolutely from records, that the diverticula may not have produced some symptoms in some patients. Four of the cases showed evidence of inflammation within the sac and a localized abscess appeared in 1 of the cases. The patient in the last case died of a purulent meningitis, hepatitis, and endocarditis.

It seems reasonable, then, to believe that when an inflammatory process occurs in a duodenal diverticulum, symptoms can and do result. There is also sufficient evidence in the literature to show that a duodenal diverticulum can cause symptoms to arise from purely mechanical reasons. Thus, if a sac is so placed as to press on a neighboring structure, such as the common bile duct, interference with the functions of the adjacent organs or pain from mechanical pressure can ensue.

As has been said before, the finding of a diverticulum in the first portion of the duodenum usually means the presence of peptic ulceration. In general, this fits in with the clinical observations. These patients usually have symptoms suggestive of peptic ulcer. In the authors' experience, however, a great many of these patients have typical peptic-ulcer symptoms. The question arises: Could the formation of a false diverticulum in this region modify the usual symptoms of duodenal ulcer? It seems clear that the patients should be treated as if they had a duodenal ulcer.

In view of these considerations, what attitude should a physician take when he is confronted with a case of duodenal diverticulum? Since no characteristic symptoms appear, he must rule out any other cause for the patient's complaints and not merely accept the diverticulum as a possible cause of the patient's trouble. The presence or absence of certain conditions will help to decide whether or not the lesion may be giving trouble. The symptoms should arise in the regions known to give rise to duodenal symptoms. MATHIAS J. SEIFERT, M.D.

Rudder, F. F.: Acute Diverticulitis of the Jejunum; Case Report. *Surgery*, 1943, 14: 921.

The author reports a case of acute diverticulitis of the jejunum in a fifty-six-year-old Costa Rican farmer.

The chief complaint was intermittent, colicky, epigastric pain without radiation, and vomiting of three days' duration. There was a past history of dull aching pain in the epigastrium about thirty minutes after a meal for two months prior to the onset of the acute attack. The significant physical findings were a temperature of 99.6°F., a flat and rigid abdomen without distention, increased peristalsis, and a point of maximum tenderness in the midepigastrium just to the right of the midline. The blood leucocyte count was 24,600, and 93 per cent of the cells were polymorphonuclear neutrophil leucocytes. Simple films of the abdomen were negative.

The pain persisted, the temperature rose to 101.2° F., abdominal rigidity became boardlike, and the blood leucocyte count rose to 49,100.

Exploratory laparotomy was done for a clinical diagnosis of perforated gall bladder. A large, acutely inflamed, solitary diverticulum of the jejunum was found about 18 in. from the ligament of Treitz

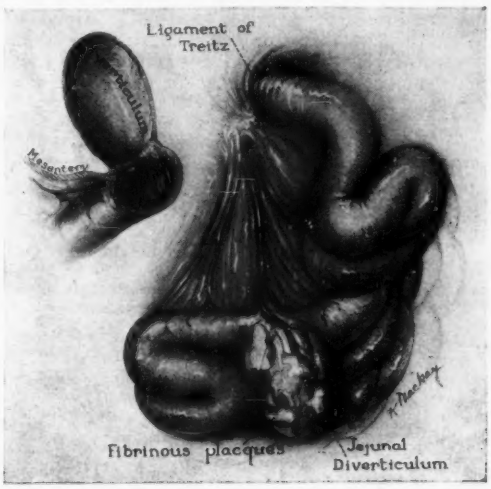


Fig. 1. Diverticulum of the jejunum.

(Fig. 1). Diverticulectomy was done, and the wall of the diverticulum was found to be lined by hyperplastic jejunal mucosa and heavily infiltrated with inflammatory cells. The postoperative course was uneventful. EDWARD GIBBS, M.D.

Kark, W.: Observations on Appendicitis with Special Reference to Conservative Treatment. *S. Afr. J. M. Sc.*, 1943, 8: 81.

Observations are recorded of 212 cases of appendicitis classified on the basis of the nature and extent of the lesion as determined by naked-eye examination at operation. Forty-two cases were described as acute appendicitis of mild degree, 34 of moderate degree, and 80 of severe degree. The last named group includes cases with general or local peritonitis and cases with abscess formation. Chronic appendicitis was encountered in 32 cases. In 24 cases there was no evidence of inflammation in the appendix and these cases were classified as appendicular colic.

The obstructive factors in the etiology of appendicitis are discussed and tabulated. The relationship of obstruction to the clinical features and to the pathological process is described.

The incidence of the clinical symptoms and signs in relation to each pathological group of the classification is recorded and the variations are discussed.

The multiplicity of etiological and pathological factors which affect the course of appendicitis modifies the clinical features and it is not surprising that patients with this disease frequently do not present a characteristic and uniform group of symptoms and signs with progression of the inflammatory process. Thus, it is folly to speak in generalizations referring to the advisability of operative treatment up to, and not beyond, a certain time limit after the onset of illness.

When the typical symptoms and signs of appendicitis are present, they are of great diagnostic value. When they are absent or if they are replaced by unusual features, they are of less significance in diagnosis, and it is dangerous to temporize with conservative therapy in such cases.

The author submits one safe generalization with but one qualification. Every case of appendicitis, with the exception of the unequivocally subsiding abscess, requires urgent operative treatment. The doubtful and stationary cases demand operation as much as the progressing cases.

EDWARD W. GIBBS, M.D.

Irwin, F. G., and Coates, G. L.: Appendicitis in the Navy. *Naval Med. Bull.*, 1944, 42: 7.

The authors report 300 consecutive appendectomies with no deaths in a naval hospital. The appendix was found to be acutely inflamed in 266 cases, and in 11 of these it was perforated. There were 34 cases of chronic appendicitis.

A typical history of appendicitis was given by 183 patients, and an atypical history by 117. Nearly one-third of the patients were operated upon within twelve hours after the onset of illness. Positive physical findings were absent in 28 patients who were found to have acute appendicitis. The writers warn that factors peculiar to the Service must be kept in mind when these cases are evaluated, to avoid overlooking appendicitis. These factors are: the robust health of the men, their tendency to report very early to the sick bay, and the frequency of atypical history and of absent or atypical physical findings.

Spinal anesthesia was used in most instances. The type of incision is not described. Various types of suture material were used. Sulfonamides were administered intraperitoneally and orally to all patients who might need help in combating the infection, and in all gangrenous and ruptured cases.

The authors contend that hazardous and ill-advised emergency appendectomy performed at sea by unqualified enlisted personnel will lose more lives than delayed surgery with substitution of the Ochsner regimen until the patient can reach a place where he may be operated upon under optimum conditions. EDWARD W. GIBBS, M.D.

Young, E. L., and Young, E. L., III: Diverticulitis of the Colon. *N. England J. M.*, 1944, 230: 33.

The incidence of diverticulosis of the colon—a prerequisite of diverticulitis—has been estimated to be between 3 and 10 per cent. A compilation of statistics shows an incidence of 5.2 per cent in 70,572 colons examined with barium and at autopsy. It is difficult to obtain significant figures on the percentage of cases of diverticulosis which progress to diverticulitis. It is usually stated that from 12 to 15 per cent do so, but in three series totaling 3,915 cases of diverticulosis of the colon the incidence of diverticulitis was 3.3 per cent.

Diverticulitis is primarily a disease of adult life.

There are two types of diverticulum, the congenital and the acquired. The former, which is rare, is a pouch consisting of all layers of the bowel wall; the latter is a herniation of the mucosa through a defect in the muscular layer. Although the cause of the acquired type is unknown, there appear to be numerous contributing and predisposing factors: (mechanical) overdistention from constipation, excess gas and feces, with pushing of the mucosa through the muscular layers, and (degenerative) changes due to age, weight, irritations, and putrefactions that cause fatty degeneration of the musculature, with loss of elasticity and proliferative trabeculations, irregularities, and fissures of the mucous membrane. Inflammation sets in when, because of irritation or occlusion by a fecalith, the narrow neck of the diverticulum becomes edematous and prevents easy emptying. The localized inflammation spreads to the adjacent segment of bowel and causes irritability, spasticity, and tenderness. Progress continues in one of two directions: acute perforation into the free peritoneal cavity with an acute diffuse peritonitis, or peridiverticulitis and pericolitis.

Diverticulitis is a disease of protean manifestations, and diagnosis is often difficult. Even the dif-

ferentiation of diverticulosis and diverticulitis is not always obvious. The former condition is supposedly asymptomatic but may be responsible for a so-called "irritable-colon" syndrome. The classic syndrome of diverticulitis consists of pain in the left lower quadrant of the abdomen, low-grade fever, slight leucocytosis, flatulence, and slight nausea, but this textbook picture is all too uncommon. Physical examination is, for the most part, negative; the temperature and white-cell count are usually normal, but occasionally they are slightly elevated. As the disease progresses, the symptomatology becomes more marked. Bleeding occurs in from 5 to 17 per cent of the cases. In addition to the history and the physical examination, the sigmoidoscope and the barium enema are used in arriving at a diagnosis. A negative examination by either method does not, however, exclude a diagnosis of diverticulitis.

Following a diagnosis of diverticulosis, measures should be instituted to avoid the factors known to predispose to diverticulitis, such as overdistention of the bowel; hard, coarse fecal material; degenerative changes; and obesity. A low-roughage diet and sufficient mineral oil or other bland laxative to promote regular, soft-formed movements eliminate the usual mechanical factors. Tincture of belladonna to relieve spasm is always beneficial. All irritative cathartics are contraindicated, especially strong saline solutions, since their prolonged use leads to hypertonicity of the rectal sphincter. All efforts should be directed toward the cultivation of regular bowel habits.

With the onset of diverticulitis further steps are indicated: a temporary soft diet to rest the inflamed sigmoid, bed rest, local heat, and antispasmodics. One of the authors (E.L.Y.) has used repeated small instillations of dilute barium with excellent results. The method in acute cases is as follows: 30 gm. of x-ray barium in 90 cc. of warm water are instilled rectally twice a week, following a cleansing enema, until subsidence; then once a week as long as the forbearance of the patient lasts. The barium fills the diverticulum, and thereby shuts out irritating feces, and is in itself mildly soothing.

About 22 per cent of cases come to surgery, but indications for surgical intervention are still unsettled and the trend in therapy is toward conservatism. There seem to be five general indications for surgery: acute perforation with spreading peritonitis, sigmoidal obstruction, formation of a fistula, localized abscess, and the inability to differentiate diverticulitis from cancer.

In the authors' series, blood was found in the stool in 26 per cent of the cases in which no cause other than the diverticulitis was present; the incidence of this condition was much higher in this series than in others, which suggests that in a true cross section of disease as seen by the general practitioner the condition should be oftener recognized and treated. When surgery is needed the simplest procedure possible gives the lowest mortality.

JOSEPH K. NARAT, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

White, F. W.: A Study of Errors in the Diagnosis of Jaundice. *N. England J. M.*, 1943, 229: 997.

The proved errors in diagnosis in 175 cases of jaundice that came to operation or autopsy were 14 (8 per cent).

The known errors, with 1 exception, were in the chronic group, and over half the errors were associated with the diagnosis of cancer, almost always with the overlooking of small or latent tumors.

It is evident that latent cancer should be considered much oftener in doubtful chronic cases. There was a tendency to make too many diagnoses of portal cirrhosis in alcoholic patients with an enlarged liver. Various cancers were called cirrhosis, but no case of cirrhosis was called cancer.

Complete obstruction of the external bile ducts was due to cancer in 96 per cent of the proved cases, and partial obstruction was benign in 91 per cent.

The essential need is to separate medical from surgical cases of jaundice. This is far more important than is the diagnosis of the specific disease of the liver; for example, it is far more important to differentiate hepatitis, the treatment of which is essentially medical, and complete obstruction, in which it is essentially surgical, than to decide just which kind of cirrhosis or complete obstruction is present.

Cases of jaundice are rarely emergencies, and it is best not to hurry the diagnosis in most acute or chronic cases, especially in the absence of serious infection (cholangitis, abscess of the liver, empyema of the gall bladder, perforation, or peritonitis), and not to trust to early impressions, which are often reversed by the course of the illness and the laboratory tests. It is especially necessary not to make the early diagnosis of acute deep jaundice a basis for early surgery, which in this series was followed by a high mortality in the wrongly diagnosed cases. A period of study, with the administration of plenty of glucose and water, protein, and vitamins, is essential in order to watch the course of the disease and to see which element predominates—damage to the liver cells, external obstruction, or hemolysis.

If unexplained jaundice appears in chronic heart disease, pulmonary infarct or hemolytic jaundice should be considered.

The diseases causing jaundice which were easiest to diagnose were toxic and infectious hepatitis, complete external obstruction, and hemolytic jaundice. Those moderately difficult to diagnose were fatty liver, acute pancreatitis, gall-bladder disease with partial external obstruction, and cirrhosis. The most difficult to diagnose were multiple lesions, cases in which the patients were extremely sick and in which the examination was therefore incomplete, and cases of tumors of the liver and bile passages.

The differentiation of hepatocellular and obstructive jaundice and of stone from cancer in the common duct has become easier in the last ten to twenty

years, but the difficulty of discovering various latent cancers causing jaundice remains.

Syphilis of the liver is less common than in the past, there being only 1 proved case. No cases of Weil's disease or chronic pancreatitis were diagnosed or found. CHARLES BARON, M.D.

Hayes, J. M.: Common-Duct Repair by Means of Vitallium Tube. *Minnesota M.*, 1943, 26: 1064.

In 1941, Pearse reported 5 cases in which repair of the common bile duct was performed over a vitallium tube. The use of vitallium was suggested since this metal is practically inert in the tissues, as has been demonstrated by its use in bone surgery. Without the use of some kind of tube to keep the ducts patent, strictures usually occur at the line of suture.

The vitallium tube devised by Pearse, and used by the author, has an internal diameter of 0.5 cm., and a length of 4 cm. The ends are flared slightly to aid in retaining the tube in place. The author reports its use in 2 patients. The results were good for a period of two years in one case and for one and one-half years in the other.

The author agrees with Pearse that this procedure should be reserved for cases in which other methods have failed. EARL O. LATIMER, M.D.

Alperovich, A., and Hours, R.: Emergency Surgery of the Biliary Tract (La cirugia de urgencia en las vías biliares). *Sem. méd.*, B. Air., 1943, 50: 1145.

The authors performed 64 emergency operations on the biliary tract, which fall into two periods. During the first period most of such operations were performed because of an error in the diagnosis, the condition being mistaken for acute appendicitis, but sometimes dangerous biliary signals indicated an operation. During the second period, which began three years ago, surgical indications have been extended.

The authors are opposed to early intervention as the method of choice in each case of acute cholecystitis, and they advocate a trial period in which conservative treatment consisting of bedrest, and the application of ice bags, enemas, and antispasmodics should be employed.

Of the 64 patients operated upon, 32 had an acute cholecystitis with stones, 3 of them with stones in the common duct; in 1 case of strawberry gall bladder no stones were present. In the remaining 31 cases, acute cholecystitis with stones and other complications were found in the following descending order of frequency: empyema, choleperitonitis, edema of the pancreas, necrosis of the pancreas, pancreatic pseudocyst, and gangrene of the gall bladder. Of the 64 patients, 54 recovered; in other words, the mortality was 15.62 per cent. The mortality among the cases with complications was 29 per cent and that among noncomplicated cases 3.03 per cent.

The collaboration of an internist with the surgeon is desirable for the treatment of cases of acute cholecystitis. Conservative treatment is advocated for the first twelve to twenty-four hours. Persistent pain, intensive peritoneal reaction revealed by the presence of a rigidity of the right abdominal wall, and tachycardia followed by a relative bradycardia are danger signals. Grave complications may be avoided if an operation is performed at a proper time, but the authors are opposed to routine employment of surgery in each case of acute cholecystitis. The simplest operation; namely, cholecystostomy, is recommended, although the authors showed that the mortality was very low after cholecystectomy, which they performed in nearly every case. JOSEPH K. NARAT, M.D.

GYNECOLOGY

UTERUS

Morton, D. G.: Carcinoma of the Uterine Cervix. Treatment and Prognosis. *West. J. Surg.*, 1944, 52: 1.

In the University of California Hospital, San Francisco, California, up until 1931, irradiation for carcinoma of the cervix was confined to that obtained by the local application of radium except for occasional x-radiation for recurrences or metastases with machines developing less than 200 kv. Since that time high voltage x-radiation has become available and has been added to the radium irradiation more or less routinely and the roentgen dose has gradually increased from approximately 1,000 roentgens each of two, four, or six fields, to 3,000 and even 4,000 roentgens to each of four fields.

If (as is shown by the figures presented) the results of irradiation are better when the two are combined than when radium alone is used, it is logical to infer that the better results are due to the control or destruction of cancer by roentgen irradiation in the areas of primary spread.

The method of applying radium during the last thirteen years has been patterned after the method used at Memorial Hospital in New York. It involves a basic dose of 4,500 mgh., 3,000 mgh. distributed throughout the cervicouterine canal, usually by a tandem of three pieces, and 1,500 mgh., given in the form of a plaque against the cervix. The total dose is achieved in three sittings, a week apart. From 100 to 150 mgm. are used in the applicators at each treatment.

For large everting growths they have adopted the popular policy of preceding the radium applications with the course of roentgen irradiation, the first radium application being made not sooner than three weeks after completion of the x-radiation; but if the growth is small in area, and particularly in older women, they often complete the radium application first, and occasionally the x-radiation is omitted entirely.

The author contends that in their clinic, at least, there is still a place for surgery in the treatment of certain cases of cervical carcinoma. He regards the controversy of radiation versus operation as unintelligent in the light of modern knowledge. He does not think there can be any such argument if the obvious fact is appreciated that operation is applicable to a small proportion of the cases only and that the majority of cases are too far advanced to make it feasible. He does not include any consideration of surgery following full irradiation except when the response to radiation appears poor, but states that experiences in examining uteri removed after full irradiation have revealed apparently well preserved cancer in a small proportion of the cases. However, he states that at present they may precede surgery by radium application for the purpose of clearing up the local sloughing growth with its infection, and although the irradiation adds to the technical difficulty of the operation, the disadvantage is more than offset by the lowered incidence of peritonitis.

The author's results are set forth in various tables too long and complicated to report here but the most significant are as follows: the five-year survival rate in 242 cases (excluding operative cases) treated by irradiation from April 1, 1931 to September 1, 1938 was 32.2 per cent. The survival rate for 264 cases, including 20 cases operated upon over the same period of time, was 35.2 per cent. From 1916 to September, 1943, radical surgery for carcinoma of the cervix was performed 100 times with an operative mortality of only 6 per cent.

The following conclusions are given:

1. Approximately 90 per cent of the cases of cervical cancer are treated best with a combination of radium and roentgen irradiation. The latter should be given first unless the growth is small in area.
2. X-radiation has added materially to the percentage of survivals, but it is dangerous and its dosage should be reduced, or it should be omitted entirely in certain types of cases.
3. A small proportion of the cases are well treated by the Wertheim operation under specialized conditions and when the patients are carefully selected.
4. Cervical cancer should not be regarded as a hopeless disease.
5. Age and the immediate gross reaction of the growth influence the prognosis in individual cases.
6. The histological type is of no value for prognosis.

CHARLES E. GALLOWAY, M.D.

ADNEXAL AND PERIUTERINE CONDITIONS

Miller, H. E.: Pelvic Inflammatory Disease of Specific Origin. *Am. J. Obst.*, 1944, 47: 245.

A study of specific pelvic inflammatory disease at Charity Hospital of Louisiana in New Orleans shows that the over-all mortality in a series of 6,184 cases reported in 1927 and 1928 was 2.5 per cent, as compared with a mortality of slightly less than 1 per cent in 3,072 cases treated at the same institution over a recent period of approximately three years, which is reported herewith.

Pelvic inflammatory disease in negro women is more frequent, is much more frequently associated with fibroids, and, because of neglect, is often much more serious than it is in white women.

Rupture of tubo-ovarian masses, although generally believed to be unusual, was observed in 8 cases in this study, in 6 of which it was fatal. Acute appendicitis furnishes the chief difficulty in differential diagnosis, and statistics show that exploration is justified if the confusion cannot be cleared up promptly. Bacteriological diagnosis, whether made with smear

or culture, is highly unsatisfactory. Except for general measures, no treatment of pelvic disease gives even approximately satisfactory results. Chemotherapy is disappointing in infections above the external cervical os, but is a useful adjunct in properly selected cases, although it is by no means free from risk. Surgery is ultimately necessary in a large proportion of cases of recurrent salpingitis, particularly in public institutions with a large number of negro patients. Conservative surgery must frequently be followed by secondary surgery, and plastic operations on the tubes have little to commend them, especially in women of the poorer classes. Drainage should be used with discretion, and appendectomy should be omitted in poor-risk cases and in those in which operation has been unduly prolonged.

An analysis of 500 recent surgical cases at Charity Hospital, compared with an analysis of 600 surgical cases from this Institution and from Touro Infirmary reported in 1927 and 1928, shows that the recent improvement in the mortality of pelvic inflammatory disease can be attributed to: the free use of fluids before and after operation, especially the parenteral administration of fluids; the free use of transfusion; the institution of measures to correct mild degrees of anemia and vitamin and protein deficiencies; the prevention of ileus by the prompt use of intestinal decompression and other measures; the prevention of pulmonary complications by various prophylactic measures; the employment of drainage only on strict indications; the performance of supravaginal rather than complete hysterectomy in poor-risk cases; and the omission of appendectomy in all but good-risk cases. Chemotherapy played only a minor part in the improved results and was not curative in any case; however, it was effective as an adjunct form of treatment in properly selected cases. The basic reason for the improvement in the preoperative and postoperative care, which in turn was the basis of the improvement in the mortality rate, was the institution of a resident system in the hospital.

EDWARD L. CORNELL, M.D.

Carey, E. L., and Gaskill, C. J.: Findings in Routine Pelvic Examinations of 1,998 Women. *Am. J. Obst.*, 1944, 47: 111.

Routine pelvic examinations were done on a group of 1,998 presumably healthy, white women (apprentice seamen W.R.) in the younger age levels. Approximately one-third of the women had some type of gynecological condition predominantly of minor nature. The incidence of major pathology as presented errs on the side of conservatism since some 10 to 15 per cent had previous pelvic examinations at the Procurement Offices, and some were undoubtedly eliminated because of major pelvic pathology. Despite this, the figures on the incidence of fibromyoma of the uterus and ovarian cyst are higher, in the authors' opinion, than would be expected. The total incidence of fibromyoma was 27.5 per 1,000, which is higher than one would expect in a predominantly young group. Nine ovarian cysts were found, 6 of which were large enough to require operation.

Naturally, the incidence of minor pathology would not be affected by any elimination due to previous pelvic examinations. The incidence of vaginitis per thousand was 13.5; that of total cervical erosions and cervicitis 122.1, cervical polyps 4.0, total malpositions 141.1, total cystic ovaries 24.0, and induration of the adnexa 8.5. These figures should represent the incidence per thousand in any similar group. Of the 1,998 women examined, 2 were candidates for major surgery. Two, because of a history of metrorrhagia, were rejected and presumably would undergo diagnostic curettage. Eight cases required removal of cervical polyps. Twenty-seven had vaginitis. Two hundred and forty-four had cervical erosions or cervicitis. According to current gynecological practice, treatment is advisable in these cases.

This large group requiring treatment (291 of 1,998) once again emphasizes the need for careful routine pelvic examinations. There is an obvious need for routine pelvic examinations not only in women of the menopausal age but also in younger women.

EDWARD L. CORNELL, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Cutler, J. W.: The Harmful Influence of Pregnancy on Advanced Tuberculosis as Modified by Collapse Therapy. *Am. J. Obst.*, 1944, 47: 1.

This presentation concerns itself with the immediate and late effects of pregnancy, and the responsibilities which follow on advanced tuberculosis in a single series of 26 white women who were treated with collapse therapy to control the tuberculosis before they gave birth to one or more children. These women were of about the same social and economic status and had been under constant clinical and roentgenological observation for varying periods during the past fifteen years. The average for the group was approximately nine years.

These 26 women had 48 known pregnancies following collapse therapy and gave birth to 40 children, of whom 36 are alive and well. Fifteen women gave birth to 1 child, 9 to 2 children, 1 to 3 children (one set of twins), and 1 to 4 children.

While the number of cases reported is too small to warrant definite and final conclusions, this study does point to certain facts:

Pregnancy, and the responsibilities which follow, can and do affect some patients with tuberculosis unfavorably; therefore, childbearing should be looked upon as a potential hazard for a tuberculous mother. Exacerbation may occur either in the early months of pregnancy or within the first few months following delivery.

Collapse therapy has definitely minimized this risk and has brought a better outlook to the expectant tuberculous mother. It has restored to her the right of motherhood. Each case, however, must be carefully evaluated on its own merits, including physiological and social factors, as well as pathological, before a decision is made for or against pregnancy.

If the disease, though advanced, is limited to one lung (as indicated by x-ray study), the diseased area is anatomically well collapsed with all cavities closed, the sputum free of tubercle bacilli, and the collapse maintained throughout pregnancy, there is little or no risk of reactivating the tuberculosis and one or more pregnancies may safely be undertaken. This is true also if there is advanced tuberculosis in both lungs, but with the disease in each lung controlled with adequate collapse therapy. Indeed, one may regard the interval of effective collapse therapy as the safest period for a tuberculous woman to marry, have children, and rear a family.

If there is disease in both lungs and only one lung, the "worse" lung, is treated with localized collapse therapy, the disease in the uncollapsed lung, although quiescent before pregnancy, may become active in approximately 30 per cent of the cases. In about half of this number, collapse therapy may be essential to control the reactivated disease in the untreated or contralateral lung. This is true even if the disease in the contralateral lung is minimal in extent, well stabilized for months or years, and the sputum negative for tubercle bacilli at the time of pregnancy. The risk, of course, is greater when the disease is more advanced and less stabilized.

The possibility of reactivating quiescent tuberculosis in an uncollapsed lung, however, is not in itself a contraindication to pregnancy. Permission may be given as long as the patient is kept under observation and is willing to accept collapse therapy when it first becomes indicated. Such women may assume the added hazard of pregnancy to their tuberculosis with the assurance that effective help is available when needed.

Pneumothorax therapy may be considered as an alternative to therapeutic abortion in the presence of active tuberculosis first recognized during the early months of pregnancy. When the collapse is good and promptly controls the tuberculosis, the woman may proceed safely to term.

Only collapse therapy which produces adequate localized collapse of the diseased portion of the lung, such as pneumothorax, maintenance oleothorax, or thoracoplasty, will prevent reactivation of the disease. Indirect collapse, such as phrenic-nerve interruption, is not enough.

Inadequate collapse therapy; that is, inability to close cavities and render positive sputum free of tubercle bacilli, may be considered the same as if no collapse therapy is employed so far as the effect of pregnancy on the tuberculosis is concerned. The majority of such patients with advanced disease do poorly and pregnancy is inadvisable.

EDWARD L. CORNELL, M.D.

LABOR AND ITS COMPLICATIONS

Gustafson, G. W.: An Evaluation of the Transverse Cervical Cesarean Section. *Am. J. Obst.*, 1943, 46: 841.

This study is based upon 208 transverse cervical cesarean sections which were performed by the author since 1931. The operations were done under average conditions in four Indianapolis (Indiana) hospitals, two of which have separate operating rooms in the maternity department for cesarean sections. Operation was elective in 105 patients; the remaining 103 patients had been in labor for periods of from one to forty-eight hours. There were 2 maternal deaths, a mortality of 0.96 per cent, and neither of these occurred as a result of infection or peritonitis. One death was due to hemorrhage, the other to cardiac failure.

Two hundred and ten infants were delivered, 7 of which failed to survive. Of these, 2 were stillborn and 5 died after birth.

Twenty-three patients had had 1 previous transverse cervical cesarean section and 3 patients had undergone 2 previous transverse cervical sections. No ruptured scars were encountered.

Substitution of the extraperitoneal operation for the transverse cervical operation would not have lowered the maternal mortality in this series.

Adequate tests of labor are safe with the transverse cervical operation. EDWARD L. CORNELL, M.D.

MISCELLANEOUS

Gellhorn, A., Flexner, L. B., and Hellman, L. M.: The Transfer of Sodium Across the Human Placenta. *Am. J. Obst.*, 1943, 46: 668.

Although the data are insufficient for precise quantitative conclusions, they indicate that in man the rate of transfer of sodium per unit weight of the placenta increases markedly as gestation proceeds. This change can be correlated with morphological changes which occur in the human placenta. Sodium appears to be transferred across a unit weight of the human placenta at about the same rate found in other hemochorial placentas at corresponding periods of gestation. E. L. CORNELL, M.D.

Maun, M. E., and Green, W. M.: Chorioepithelioma with Regression of the Primary Uterine Tumor. *Am. J. Obst.*, 1943, 46: 738.

A twenty-two-year-old white woman, a nullipara, delivered a normal male infant at term. The gestation and delivery were normal. The placenta was normal to gross examination. The woman was seen six weeks later for a routine post-partum examination. She had no complaints, and pelvic examination revealed no abnormalities.

Three months later the patient was admitted to the hospital because of complaints of progressive weakness, and intermittent chills and fever, all of which had been present for two weeks. On examination the temperature was 102.6° F., the pulse 120, respirations 30, and blood pressure 118/68. All x-ray and laboratory findings were negative, except the blood count which showed marked anemia.

One month later there was tenderness in the right upper quadrant. The liver could be palpated 5 cm. beneath the costal margin. Free fluid was present in the abdominal cavity. The patient was given blood transfusions, but she continued to fail rapidly, and expired.

At autopsy a large tumor mass could be seen beneath the capsule of the right lobe of the liver, and several perforations of the capsule were present on the anterior surface. The right lobe of the liver was almost replaced by the very large tumor mass bulging from the cut surface and measuring 15 cm. in diameter. In the fundus of the uterus there was a raised soft hemorrhagic mass measuring 2 cm. in diameter and 1 mm. in thickness. On palpation, it was extremely soft in consistency and grossly did not appear to penetrate the uterine wall. On microscopic examination of the liver viable trophoblastic cells could be identified only at the edge of the tumor; these showed marked pleomorphism. The trophoblastic cells were found around and within the abundant vascular spaces present. No teratomatous areas were seen in the numerous sections which were examined.

Numerous blocks were taken from the lungs, but careful search revealed no trophoblastic tissue. Examination of the sections in approximately the midportion of the uterus showed the endometrium to be thin with preservation of only the basal layer. It further showed a mild decidual reaction. The vessels of the uterine wall showed retrogressive changes with marked proliferation of the intima, narrowed irregular lumens, and a deposit of homogeneous hyaline material beneath the endothelium. A careful study of the vascular lumens and the entire uterine wall revealed no trophoblastic cells. The hemorrhagic mass seen on gross examination proved to be partially necrotized and contained shadows of decidual cells. This mass apparently represented abnormally retained placental tissue that may have served as the *situs locum* of the uterine tumor. The genesis of extragenital chorioepitheliomas has provoked the interest of clinicians and pathologists.

EDWARD L. CORNELL, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY, AND URETER

McKim, G. F., Smith, P. G., and Rush, T. W.: Twelve-Year Survival with One-half of One Kidney. *J. Urol.*, Balt., 1943, 50: 769.

It is well known that the amount of renal parenchyma present in the normal adult is greatly in excess of the amount that is necessary to insure prompt discharge of the renal responsibilities of normal life. It is likewise well known that life can be maintained after the major portion of the renal parenchyma has been rendered inactive by surgery or by disease such as polycystic disease, chronic nephritis, bilateral hydronephrosis, or pyonephrosis. Undoubtedly there are many nephrectomized individuals who are successfully maintaining life although their remaining kidney is partially destroyed by disease.

Life has been successfully maintained in laboratory animals for long periods of time after the surgical removal of 75 per cent of their renal parenchyma, but we know of no recorded instance in the human being in which both a nephrectomy and a heminephrectomy have been performed and were followed by successful results. For this reason the authors report the case of a woman who has lived twelve years with one-half of a kidney. During this twelve-year period she has led a normal life, and, with the exception of having undergone a pregnancy, a cholecystectomy, and recently the menopausal cycle, has been perfectly well. JOHN A. LOEF, M.D.

Morison, D. M.: Ureteritis: A Clinical Survey Based on 147 Cases. *Edinburgh M. J.*, 1943, 50:661

The term "ureteritis" is used to designate a lesion of the ureter which is not yet fully understood. From the standpoint of pathology the lesion may be regarded as relatively trivial in that it may not cause embarrassment to the conducting system of the urinary tract. Its recognition by intravenous and retrograde pyelography is not always certain.

It is apparently due to a localized spasm of the ureter and is usually intermittent in character. The pain consequent to this spasm is sufficiently distressing to cause advice to be sought. If the areas of spasm involve the lower abdominal or upper pelvic ureter the attacks of pain frequently offer a diagnostic problem.

Irritability of a ureter may be referred to its entire length, or it may be localized in certain zones. It is only in a few marked cases that there is a diffuse ureteritis. It is more usual to find a zone of ureteritis referred to those areas of the ureter which physiologically show narrowings.

Ureteral spasm occurring in these zones gives rise to pain which is referred to definite areas of the abdomen. Pain arising from Zone 1, the pelvoureteral junction, is referred to the subcostal area and extends around to the loin behind. Pain from Zone 2, where the ureter crosses the iliac vessels, is referred to just below and lateral to the umbilicus. Pain from Zone 3, where the ureter is in apposition with the broad ligament in the female and the vas deferens in the male, is referred to the inguinal region. Pain from Zone 4, the portion of ureter which passes through the bladder wall, is referred to the area immediately above the symphysis pubis.

The pathology of ureteritis, or ureterospasm, has not been determined. The nature of ureteritis is such as to preclude the removal of tissue for histological study. The intermittency of the pain would suggest that the affected zone of ureter must contain some element of an inflammatory nature so as to render it hypersensitive and liable to enter into spasm whenever a suitable stimulus occurs.

The diagnosis of ureteritis depends on the reproduction of the pain as to character and location during cystoscopic investigation. Consequently the full co-operation of the patient is required. For such cystoscopy a general anesthetic or deep hypnosis by premedication is contraindicated. On bladder inspection a cursory view will usually disclose no obvious pathology, but on more careful scrutiny, though the bladder walls may be completely normal, a study of the bladder neck will show a mild degree of contracture. This will be accompanied by some hypertonicity of the trigone and slight accentuation and thickening of the interureteral ridge. The ureteral openings are usually negative as to position, but both will show a certain degree of raising or pouting of their margins, and around them a stippling of the mucosa will be observed as well as an increased hyperemia of the trigonal mucosa. These findings are to be expected in cases of low ureteritis, involving that portion of the ureter which enjoys the same nerve supply as the trigone and bladder neck.

Visual inspection having been completed, ureteral catheters are held in readiness for introduction, but before any ureteral instrumentation is done the patient is asked to state at once should he feel any difference in the way of discomfort, from the sensation he has with the cystoscope in situ. It is advised that at this point in the examination, the bladder, if it has been fully filled, should be slightly decompressed so as to eliminate any possibility of mixed interpretation, and remove the natural desire to void.

The catheters are now taken and each in turn is gently inserted into the opening of the ureters. As the tip of the catheter is slowly inserted into the ureteral meatus and gently advanced, the patient will at once state that a desire to void has been set up. This would immediately indicate to the operator that there is a low ureteritis on that side. As the ureteral catheter is left in situ the desire tends to diminish, and if it is not marked, total investigation of the ureter may be proceeded with. The catheter is now advanced to the full extent, and any

further areas of discomfort on that side are located with the help of the patient. If there is diffuse ureteritis, pain will next be referred to the region slightly below and lateral to the umbilicus as the catheter is advanced, and then to the subcostal area radiating around to the flank. If a ureteritis of such marked degree is present, one would anticipate with almost certainty that drainage is impaired and aspiration will reveal residual urine in the kidney.

When a ureteritis is less marked in degree the passage of a straight ordinary ureteral catheter may not give any positive finding and the patient may seem undecided that the discomfort produced is similar to the pain complained of. In these instances it is essential, before stating that no ureteritis is present, that the ureters be tested with bulbed bougies.

TREATMENT

1. Ureteral dilatation. The following is the routine employed. An F_5 ureteral catheter is first passed up the full extent of the ureter to the renal pelvis, and the residual urine, if any, is removed by aspiration, and the quantity noted. The amount of residual urine gives an indication as to the amount of improvement in renal drainage that is being obtained. After this, 2 cc. of 2 per cent argyrol are instilled into the renal pelvis and down the ureter as the catheter is withdrawn. Bulbed bougies are now introduced, commencing with a size F_7. The bulb is passed up and will probably meet with slight obstruction at the transmural portion of the ureter, and if this is the site of the main lesion the patient's symptoms of suprapubic pain will at once be elicited. After passing through the transmural portion and reaching the broad ligament or vas zone, resistance may again be felt, and as this is overcome the patient will immediately indicate pain in the corresponding inguinal region. As the bulb is further advanced the narrowing at the common iliac region will give rise to discomfort below and lateral to the umbilicus, and as the bulb reaches its ultimate limit, the pelvoureteral zone, a definite subcostal discomfort will be set up. Should the F_7 bulb pass relatively easily through the succeeding areas of narrowing, a bulb F8 is tried, and sufficient pressure exerted on it to enable it to pass through the various zones as previously determined.

2. Short-wave diathermy. In cases of markedly nervous patients with an extremely sensitive urinary tract, it will be found that definite benefit will result in submitting them to a preliminary course of short-wave diathermy directed over the site of pain. This relaxes the spasm and renders the ureter more amenable to subsequent dilatation.

3. Denervation of the ureter. In cases which have not responded to full courses of ureteral dilation and short-wave diathermy, and severe pain continues, denervation of the ureter should be done. This has been carried out in a selected series of cases with complete relief of pain and no alteration in ureteral function. JOHN A. LOEF, M.D.

Ainsworth-Davis, F. C.: Calculi Impacted in the Lower Fourth of the Ureter: Their Removal with the Ureteral Corkscrew. *Brit. J. Surg.*, 1943, 31: 34.

Through the medium of ureteral meatotomy and a specially modified ureteral corkscrew, the author has been able to remove 19 of 20 calculi impacted in the lower fourth of the ureter. The patients comprised R. A. F. personnel and showed no symptoms of acute obstruction of the upper urinary tract. It was believed that in all nonobstructed cases of stone in the lower ureter, instrumentation should be given a trial before open operation was undertaken.

In addition to manipulation with the ureteral corkscrew, the corkscrew is often left *in situ* and a small weight extension is applied to the distal end of the instrument by means of a pulley attached to a bed cradle. A string is provided whereby the patient himself can raise the weight and so remove its entire pull should the traction cause extreme discomfort. The corkscrew is marked at its point of emergence from the urethra, so that the effect of the extension can be gauged. The entire procedure of cystoscopy, ureteral meatotomy, and insertion of the corkscrew is done under pentothal anesthesia, followed by gas and oxygen. Premanipulation and postmanipulation x-rays are taken as a guide.

The method described was used in 20 patients in a period of twelve months. In all cases the stone was impacted in the lower third of the ureter above the intramural segment. In 2 cases the stone was removed at the time of initial instrumentation. In 3 cases, the calculus was removed after forty-eight hours of weight extension, in 6 it was extracted after a second attempt, and in 8 the stone was passed naturally within three weeks of instrumentation. In the 1 unsuccessful case, two attempts to pass the corkscrew having failed, the stone was removed by operation.

When the corkscrew is left *in situ* with traction, and there is no appreciable movement of the instrument after forty-eight hours, the patient is given pentothal anesthesia, a cystoscope is passed, and removal is undertaken under vision. It has been found that the stone may be removed while enmeshed in the spiral or it may be fragmented during its removal. In a few cases all attempts to pass the corkscrew beyond the stone will fail, but if back-pressure signs are absent, another attempt should be made in a few weeks. Routine urological investigation should be carried out in all cases after a period of one month to establish recovery of the upper urinary tract and also, if possible, to discover the original cause of the calculus so that it may be eradicated. ARTHUR H. MILBERT, M.D.

Turner, G. G.: Transplantation of the Ureters into the Large Bowel. *Brit. M. J.*, 1943, 2: 535.

A brief review of the entire subject of ureteral transplantation based on personal observations is presented. Of an original group of 17 cases, 9, in which the patients survived to date for from sixteen to thirty years since operation, are reported. None

of the patients who survived the immediate operative period has subsequently died because his ureters were transplanted.

Until recently, the author believed that it was safer to transplant one ureter at a time. With better understanding of the problem, simpler technique, and better aftercare, he now believes that simultaneous transplantation, except in children, seems the procedure of choice. Even in children the hazards of a second anesthetic may perhaps balance the only slight extra risk of the double transplantation.

The technique is now carried out without any special apparatus. Clamps are not used either for the ureter or the colon. Coffey's tubes are no longer employed and Mayo's catgut guide has been discarded. The main point is to make an oblique implantation into a submucous bed in the bowel without kinking or compression and with due regard for the blood supply of the ureter. Compression from too tight suturing or from hematomas or traumatic edema is probably the most harmful thing that can occur. Fine 3/0 or 6/0 chromic catgut is used throughout and no drainage is employed.

The operative technique is presented in detail together with the immediate postoperative progress and treatment. Concerning the mortality, the rate depends to a considerable extent on the condition demanding the operation. In the nonmalignant cases, and especially in congenital deformities, it should be about 5 per cent, but in the malignant cases such a low rate is not to be expected if the possible advantages of the operation are to be offered to the greatest number of sufferers. In children some deaths have been due to chest complications and to the exanthemas, and the author stresses the wisdom of choosing the summer months for operation and of keeping the patients in the hospital two weeks before operation.

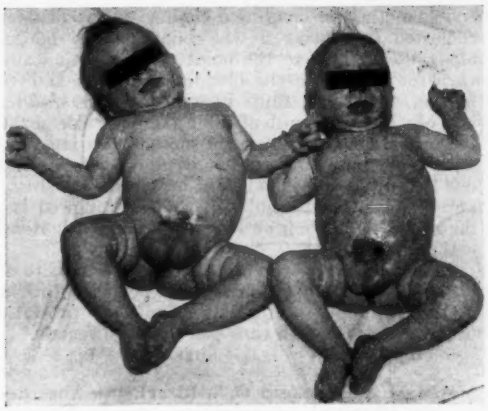
There is no stated time for dealing with the second ureter. The interval must depend on the progress made after the first intervention. If uneventful, three weeks have proved a satisfactory interval. The surgeon must bide his time. The chief error is to reoperate too soon.

A widening scope is seen for transplantation of the ureter into the bowel. For many cases of malignant disease of the bladder, total cystectomy after transplantation of the ureters holds out the best prospect of long palliation or even cure. In cases of extension of malignant disease of the cervix to the adjoining bladder, when radium and hysterectomy are impractical, transplantation and subsequent total hysterectomy and cystectomy offer a ray of hope. The operation may find use in certain intractable cases of vesicovaginal fistula, and, rarely, in severe traumatic injuries to the urethra usually with a fractured pelvis. ARTHUR H. MILBERT, M.D.

BLADDER, URETHRA, AND PENIS

Higgins, C. C.: Exstrophy of the Bladder in Twins. *Cleveland Clin. Q.*, 1943, 10: 138.

A preliminary report of identical twins born with exstrophy of the bladder is presented. The anomaly



occurs once in approximately 40,000 births, with a ratio of 7 males to 1 female. In a review of the literature, the author was unable to find a report of the occurrence in twins.

As the various theories advanced to explain the cause of the condition (mechanical, pathological and embryological) were reviewed, it was believed that the presence of the anomaly in twins would seem to give credence to the embryological theory of the development of exstrophy of the bladder rather than to the mechanical or pathological theory.

The twins were identical males, born three months prior to their admission to the hospital, there being one placenta and two cords. The two siblings were normal in every respect, and there was no evidence of a similar anomaly in the family history. The birth weight of the twins was 5 lb. 4 oz., and 4 lb. 12 oz., respectively, and at three months one had gained 5 lb. and the other 4 lb. Gain in weight had been retarded by frequent stools since birth. Both were malnourished and dehydrated when examined. One had complete exstrophy of the bladder with an associated hypospadias and a bilateral indirect inguinal hernia, with normal descent of the testes. The same condition was present in the other child except that the left inguinal hernia had become strangulated six weeks after birth and was repaired. Laboratory studies were normal in both and a complete urological survey revealed no pathology in addition to the previously mentioned congenital anomalies.

ARTHUR H. MILBERT, M.D.

Dourmashkin, R. L.: Complete Urethral Occlusion in the Living Newborn. Report of 5 Cases. *J. Urol.*, Balt., 1943, 50: 747.

In this article the author reviews the literature on 50 cases of urethral occlusion in the living newborn (46 males and 4 females), and reports 5 personal cases—a total of 55 reported cases. The cases are tabulated as to the point or extent of urethral occlusion, therapy, and mortality. In addition, 32 cases of urethral occlusion in the stillborn are analyzed.

The method of creating a channel to the bladder consisted in passing a whalebone filiform bougie along the urethra to the point of obliteration and then forcing it into the bladder with a to-and-fro motion, or boring action. Entrance into the bladder was heralded by a gush of urine along the side of the filiform. In each instance the method was attended with immediate success. One child, now ten and one-half years of age, is free of any urinary disturbance. Whenever possible, the author followed the filiform with a No. 4 or No. 5 olive-tipped ureteral catheter.

In the author's series of 5 cases, the exact site of occlusion was as follows: the entire penile urethra in 2, the cavernous urethra in 1, and the prostatic urethra in 1; the fifth case was that of a female.

ROBERT LICH, JR., M.D.

Magid, M. A., and Culp, O. S. Ideal Penile Anesthesia Obtained by Injection of the Corpora Cavernosa. *J. Urol.*, Balt., 1943, 50: 508.

Finding that most of the popular types of local anesthesia for circumcision in the adult were not completely satisfactory, the authors produced ideal anesthesia of the entire penis and anterior urethra by injecting 10 cc. of 1 per cent or 2 per cent procaine into each corpus cavernosum just below the symphysis pubis. This method, which the authors do not claim as original, was found to be dependable, simple of administration, and dramatic in effect; the anesthesia continued from three to seven hours, without distortion of the anatomic landmarks, and without any systemic drug reactions or disturbances in the physiology of the penis in more than 300 clinical applications.

With a No. 23 gauge needle on a 20 cc. Luer syringe, a quick stab is made lateral to the midline vessels into one corpus. The needle can be felt to penetrate the dense coat of the corpus. Before the injection, aspiration is attempted and if blood is obtained, another portal of entry is tried. This is usually unnecessary. A total of 10 cc. of 2 per cent procaine containing 3 drops of epinephrine per 30 cc. is then injected into the corpus. If the point of the needle has been inserted into the proper depth, no force is required for the injection and no swelling of the area will result. The process is repeated in the opposite corpus cavernosum. Usually the anesthesia is almost instantaneous, but occasionally the operator must wait from ten to twenty minutes for complete loss of sensation in the prepuce.

With this technique, the authors claim to produce anesthesia of the entire penis and anterior urethra. The skin of the scrotum and perineum is not affected, but the skin overlying the pendulous segment of the penis is rendered insensitive. The urethral anesthesia usually extends to the region of the external sphincter and the urethra is insensitive to all pain except stretching. This method of anesthesia has been employed in routine circumcision, operative and manual reduction of severe paraphimosis, excision of tumors in the distal portion of the penis, fulguration of condylomas and verruccae, meatotomy, and closure of penile urinary fistulas.

The authors state it is difficult to explain anatomically why this type of injection produces such complete anesthesia. According to anatomists, the penis derives its nerve supply from the pudendal nerve and the pelvis plexuses. In the light of the accepted nerve supply to the penis, injection into the corpora cavernosa cannot be explained unless some of the fluid diffuses outside of the corpora beneath Buck's fascia.

Fear of systemic reaction to the procaine after intracorporal injection has caused some clinicians to be hesitant about adopting this form of penile anesthesia. Despite the known vascularity of the corpora, no reactions have occurred in more than 300 patients. The slow absorption of the drug appears to account for this finding. In association with diodrast, instead of procaine, subsequent x-rays of the injected area showed this slow rate of absorption.

ARTHUR H. MILBERT, M.D.

MISCELLANEOUS

Hollander, F., Kriss, B., Klempner, E., and Frank, R. T.: The Constancy of Androgen Concentration in the Urine. *Endocrinology*, 1943, 33: 217.

In the course of androgen bioassays performed on a consecutive series of urine specimens from each of several cases, it was noted that the daily excretion of androgens varies considerably from time to time in one individual. On the other hand, when the androgen excretion was tabulated on a per liter basis, i.e., as concentration, the authors observed a notable degree of constancy for any one case. This observation differed so greatly from what is generally accepted that it led to a more careful study of the relation between androgen excretion and urinary volume. A review of the literature for the last five years revealed no thorough investigation of the problem.

Each of 9 human subjects, normal from the standpoint of kidney function, was studied by determining the biologically active androgen content and urinary volume in a series of consecutive three-day specimens of urine, collected for a period of approximately one month. In 3 of these cases, the urinary output was varied throughout the period of study by forced and restricted fluid intake.

Androgen content was determined by the chick-comb method and the results were expressed in terms of output per liter of urine (concentration) and in output per twenty-four hours.

The results showed that the concentration of biologically active androgens in the urine is constant within the limits of reliability of the assay method, and independent of the daily urine output, even under forced and restricted fluid intake.

Contrary to the foregoing, the androgen output per twenty-four hours showed considerable variation. The standard deviation for any one set of these values was invariably greater than for the concentration data, the difference being as much as four-and-

one-half-fold in an extreme case. However, these variations in daily output of androgens were not irregular but paralleled the daily output of urine. The correlation coefficients were 0.95 or greater in 5 of the 9 cases, and never fell below 0.72. This finding was contrary to the report of Oesting and Webster.

Such constancy of concentration is not in accord with the behavior of any other urinary constituent. Further study of this problem is necessary before any definite conclusion can be drawn concerning kidney function in relation to androgen excretion.

ARTHUR H. MILBERT, M.D.

Kirwin, T. J., Lowsley, O. S., and Menning, J.: Effects of Pyridium in Certain Urogenital Infections. *Am. J. Surg.*, 1943, 62:330.

A study was made of 118 cases of urogenital infections. Routine pyridium therapy administered for a period of two weeks resulted in a significant reduction of the organized sediment in 65, or 55.1 per cent, of the cases, together with relief of the characteristic symptoms of urogenital infection. In the remaining 53 cases, relief of symptoms occurred, except in a few exceptions, although there was no concomitant reduction in the organized urinary sediment.

Relief of the distressing symptoms characteristic of urogenital infections occurred as follows: pain on urination was alleviated or abolished in 95.3 per cent of the cases; burning on urination was relieved in 93.6 per cent of the cases; the intervals between bladder evacuations became normal, or were greatly extended in 85 per cent of the cases; and nocturia was eliminated or reduced in 83.7 per cent of the cases.

Careful observation revealed no toxic effects from the routine administration of this drug, in the dosage of 2 tablets (0.1 gm. each) three times a day, throughout a minimum period of two weeks.

CONCLUSIONS

Pyridium has proved to be a valuable addition to the physician's weapons against infections of the urinary tract.

In a significant number of cases, it has been found to be effective in reducing the amount of organized urinary sediment, and especially in relieving the characteristic symptoms of urogenital infections, such as dysuria, burning, frequency, and nocturia.

Relief of symptoms occurred in most instances even when no decrease in the amount of organized urinary sediment was observed.

Pyridium may be administered in therapeutic dosage with complete safety throughout the course of common urogenital infections.

JOHN A. LOEF, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Steinsleger, M., and Slullitel, I.: Angiomas of the Knee (Angiomas de la rodilla). *Rev. ortop. traumat.*, B. Air., 1943, 13: 1.

This article presents the complete case histories of 2 patients with primary angiomas of the knee. The first patient was a child fourteen years of age. The swelling was painless and for a time interfered with flexion of the knee. On palpation no point of tenderness nor any increase of fluid was observed. X-ray examination of both knees was negative.

Under local anesthesia a vertical incision was made over the internal aspect of the knee. On disarticulation a small mass adherent to the capsule by means of a pedicle was found and excised. Exploration of the knee disclosed no other pathological changes. The histopathological report was consistent with a sclerotic type of angioma.

The second patient was twelve years old, had had a normal birth, and had begun to walk at fourteen months, although there was some difficulty, particularly the knocking of the left knee. Pain was only experienced occasionally.

Prior to coming under the care of the surgeon, the patient was pushed down some steps by a playmate and landed on the floor on the left knee. For some hours after there was pain and inability to walk.

Examination showed a decided anterolateral curvature of the left knee region. The knee was globular in shape and contained free fluid. On palpation it felt warm, and it was painful on passive motion. Flexion was limited and the patient could not walk without aid.

Roentgen-ray examination of both knees revealed slight irregularities of the femoral and tibial epiphyses and of the shaft.

An arthrotomy was done, and when the capsule was opened a large diffuse firm dark mass of clotted blood was found and removed in its entirety. The mass appeared to be an angioma infiltrating into the superficial articulations of the femur, tibia, and shaft.

The histopathological studies disclosed a cavernous type of angioma.

Examination of the first case after two years revealed the patient to be perfectly cured without any limitation of motion or pain in the knee-joint region. The authors attribute their success in both of these cases to the total extirpation of the tumors.

In the discussion of these cases it is claimed that primary articular angiomas are rare. They are usually benign lesions and may exist as circumscribed or diffuse masses. Some authorities consider them congenital, whereas others think they are of traumatic origin; however, they do not deny an underlying congenital contributory factor.

The clinical symptoms vary and may be traced back as far as early infancy, but usually attention is directed to the condition following trauma to the affected part.

The diagnosis may be difficult, requiring roentgenography and exploratory puncture at times. The circumscribed type of the disease is confused with fracture and subluxation of the menisci, whereas the diffuse type is mistaken for tuberculosis. Rheumatoid arthritis and chronic arthritis following trauma have likewise been wrongly diagnosed as angioma.

The treatment is surgical and only complete extirpation can insure against recurrence. Roentgen-ray therapy and radium have been used but have been found successful only on superficial lesions.

STEPHEN A. ZIEMAN, M.D.

Kraft, E.: Epidermoid Carcinoma of the Tibia: Report of 2 Cases. *Am. J. Roentg.*, 1943, 50: 602.

There are two types of invading squamous-cell carcinoma of the tibia: (1) carcinoma arising in a chronic ulcer, and (2) carcinoma originating in a fistulous tract.

Crural ulcers and fistulas may persist for a long time without showing any malignant degeneration. These tumors, even in an advanced stage, are characterized by a low grade of malignancy and practically never form metastasis. Malignant degeneration is characterized by rather rapid spreading of chronic stationary ulcers and fistulas and the secretion of foul-smelling pus. Wartlike or cauliflower-shaped masses finally develop in the center of the lesion. These developments are associated with loss of weight and strength and secondary anemia. Roentgen findings of ulcer carcinoma are characterized by the "scooped-out" appearance of bone with extensive osteolysis and, finally, by pathological fracture. Periosteal elevation might be observed proximal to the lesion.

Fistula carcinomas are more difficult to diagnose by their roentgenographic appearance. Eburnated bone due to chronic osteomyelitis shows rapidly progressing decalcification and surface erosion, and, finally, pathological fracture occurs. Biopsy should be done before radical operation is taken into consideration. In deep-seated tumors the specimen for the biopsy must be taken from the depth of the lesion.

One case of ulcer carcinoma, and 1 case of fistula carcinoma, roentgenograms, and a review of literature are presented. GEORGE I. REISS, M.D.

FRACTURES AND DISLOCATIONS

Moore, J. R.: Delayed Reduction of Fractures. *J. Bone Surg.*, 1944, 26: 151.

This study is based upon 7,009 fractures. Reduction was required in 5,608 fractures.

Immediate reductions of simple fractures numbered 253, and of compound fractures, 315. Delayed reductions of simple fractures numbered 4,936, and of compound fractures, 45. All of the delayed reductions were done from four to eleven days after fracture.

1. All fractures are examined immediately for nerve and vessel injury, and for such complications as head, spinal-cord, and internal injuries. The treatment of these major problems is instituted immediately by the department concerned.

2. All fractures of the long bones are immobilized immediately in plaster-of-Paris splints which routinely include the joint above and the joint below.

3. Roentgenograms are taken at the convenience of the roentgenographic department either immediately or the following day.

4. One day a week is set aside for the reduction of fractures.

Following immobilization at the time of admission, the patient is kept under observation in the accident dispensary for an hour, and is then allowed to return home, or is admitted to the hospital, the choice depending upon the absence or presence of complications, and the facilities for care at home. He is instructed to report on the day set aside for reduction, and special emphasis is placed upon preanesthesia preparations. On the morning of the reduction, a cylindrical section of plaster, from 3 to 4 in. in width, is removed at the site of the fracture in fractures of the long bones. If traction is required to maintain reduction, a single pin is inserted in each major fragment. The temporary splints employed in other types of fractures are removed. The latter fractures are reduced and are subsequently splinted according to the standard methods. Reduction is uniformly successful, provided complete muscle relaxation is obtained. Generally speaking, the effort required for reduction is greater than that observed in immediate reduction.

The reduction of fractures may be delayed. The ideal time for delayed reduction is between the fourth and eleventh days. Complete immobilization in plaster should precede delayed reduction.

The value of immediate immobilization cannot be too strongly stressed. Fourteen hundred and one fractures in the present series required no reduction, merely immobilization. The author believes that the immediate immobilization upon admission partially accounts for the lack of displacement, and, therefore, the lack of need of reduction in this large percentage of cases.

However, it must be noted that no fractures were immobilized with the skin under tension, the alignment being corrected sufficiently to eliminate skin necrosis (secondary compounding).

Compound fractures (exceptions noted), simple dislocations, compound dislocations, and fractures complicated by nerve or vessel injury should be regarded as emergencies. The time required for repair in the group of delayed reductions would seem to date from the time of fracture, rather than from the time of reduction, since additional delay was not observed. Union and function appear to be unhampered. Delayed reduction provides the opportunity for excellent teamwork. The best trained individuals are readily available for all purposes. The patient is adequately prepared for anesthesia. Medical students have the opportunity to observe fractures before, during, and after reduction. The author has not had the opportunity of running a parallel series over the eight-year period, but, by comparing the results of this delayed-reduction group with those of the previous, admittedly small, immediate-reduction group, he finds there is little doubt as to which are better. Delayed reduction is not urged here. If teams which provide well trained supervision are available for immediate reduction, immediate reduction should be done. In the localities where well trained supervision is not at hand, it would appear that delayed reduction is by far the better procedure. In conclusion, one might say in defense of delayed reduction, "A well-supervised delayed reduction is better than a poorly supervised immediate reduction."

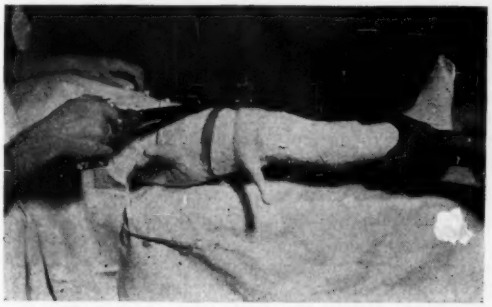


Fig. 1. The pins have been incorporated in plaster, and the cylindrical section has been cut out; the reduction is in process.

In a discussion of this article, KELLOGG SPEED remarked that he had heard Moore give a talk along this line, and that everyone in the audience appreciated his magnificent results. Speed's impression was that many of the results occurred in children in whom one invariably expects to get good results. He agreed with Smith-Petersen that it would be very unwise to teach this method or advocate it in general for practitioners. When the average run of fractures in the country are analyzed, Speed wonders how many are reduced immediately? He ventured to say that it is a very small percentage. A great many of them lie six, eight, or ten days, either for consultation reasons or because there is no help available, and yet the results are good. He believes Moore put it rather strongly, when he bluntly said we must delay. Speed agreed with Bennett that it is far better to have a good man reduce a fracture after a period of several days than to have a poor man do it immediately.

J. ALBERT KEY felt that Moore's method was one of expediency rather than of choice. He could not believe that a patient is as comfortable in a cast or without a cast, with a fracture not reduced, as the same patient would be with the same degree of fixation if the fracture were reduced. If this is not a method of expediency, there should be an optimum time; that is, the fracture should not be reduced on Tuesday but at the optimum time. He stated that Moore's results were beautiful; they were better than Key's. On the other hand, he thought they were much better than he could get with his method. In Key's opinion, fractures that have gone for several days with a lot of swelling are more difficult to reduce than if they had been reduced immediately. Part of Moore's success is due to a principle, which all realize but rarely use,—if each fragment is immobilized in a cast and then the cast is cut, reduction is easier. This is true especially if one wants to put in a couple of pins and then fix those in the cast. Personally, Key is going to continue with the method he has always used; that is, he prefers to see the patient as soon as possible after the accident, and reduce the fracture immediately.

WALTER P. BLOUNT commented to the effect that a fracture of the femur in a child has an average overgrowth of ½ in. in the first year. If the fracture is accurately reduced as to length, the femur is likely to be ½ in. too long. If two pins are inserted, the overgrowth is going to be increased. Blount stated that the use of these pins in children should not be encouraged. The overgrowth is permanent. Skeletal fixation is rarely needed in a child, and it introduces an added risk. ROBERT P. MONTGOMERY, M.D.

Wammock, H., and Arbuckle, R. K.: Fractures of the Rib Cage Following Interstitial Radium Therapy for Cancer of the Breast. *Am. J. Roentg.*, 1943, 50: 609.

The effect of roentgen and gamma irradiation upon bone is not well understood. In 1903 Perthes called attention to the influence of roentgen rays and radium on the epiphyseal growth of long bones. Recamier and Tribondeau in 1905 demonstrated experimentally that bone growth could be retarded by a roentgen-ray dose so small that it caused no change in the bone cells. In 1910 Cluzet demonstrated that irradiation inhibits or delays callus formation after a fracture. In 1922 Regaud called attention to bone necrosis following roentgen and gamma irradiation. The conclusions reached by Ewing in 1926 from a study of 3 cases of bone necrosis after heavy irradiation for bone tumor are significant. He reports as follows:

1. Moderate irradiation greatly reduces the growth capacity of bone cells, and the bones are united after fracture by the formation of an unusually hard callus.

2. After more severe irradiation, such as that which falls within the upper limits of therapeutic measures now commonly employed, there may be established a progressive productive osteitis which may cause marked thickening of the shafts, mostly at the expense of the marrow cavity, and in the case of cancellous bone may largely replace the fat and cellular marrow by poorly formed and brittle bone or calcified osteoid tissue.

3. Severe therapeutic irradiation of bone produces a peculiar change in the structure and composition of lamellar bone which is shown by increased fragility and a marked tendency to spontaneous fracture. Under favorable conditions, however, the fractures may slowly heal. After such irradiation the bone is nearly devoid of circulation, and the periosteal vessels are generally much sclerosed.

4. Heavy irradiation renders the shaft of a bone very brittle and prone to spontaneous fracture; the periosteum is injured and a persistent mass of indolent tissue prevents the restoration of function to the limb.

In 1934 Colwell and Russ wrote: "Adult bone is relatively resistant to x-ray and injuries from this cause are rare."

A full appreciation of this irradiation effect depends upon an understanding of the anatomy and physiology of the structures involved.

The ribs are elastic arches of bone which form a large part of the thoracic cage. On the inferior border of the shaft is a groove for the intercostal vessels and nerves. Within the groove are seen numerous small foramina for nutrient vessels which traverse the shaft obliquely from before backward. The blood supply of the ribs is derived from the internal mammary artery which supplies the anterior intercostal branches, and from the thoracic aorta, with the exception of the two superior intercostal spaces, which are supplied from a branch of the subclavian artery.

The physiology of bone is a little less well known than the anatomy. Bone contains the great calcium and phosphorus reserve of the body, a reserve which is continually being drawn upon or added to, so that the structure of bone is not fixed and permanent. It is composed of living cells and a hyaline matrix impregnated with calcium salts. The vital character of bone is illustrated by the words of Sir Charles Bell, written more than a hundred years ago: "Scrape a bone and its vessels bleed; cut or bore a bone and its granulations sprout up; break a bone and it will heal; burn it and it dies."

All bone, wherever found, is formed through the activities of specialized connective-tissue cells, the osteoblasts. The methods of bone formation are: (1) direct or intramembranous, (2) endochrondal, and (3) periosteal. The ribs develop by the intramembranous and periosteal methods, whereby the bone matrix is formed by the osteoblasts directly within the layer of young connective tissue.

Knowledge of changes in bone resulting from interruption of the circulation has made slow progress. Phemister offers a number of reasons for this: (1) the absence or mildness of immediate symptoms from simple interruption of the circulation; (2) post-mortem studies of the skeleton are less com-

mon and less extensive than those of the viscera; (3) operation offering a chance for pathological examination is seldom indicated with most forms of aseptic necrosis; and (4) the roentgen signs of the condition, which are late in appearing, were long confused with those of other chronic lesions.

There are two chief factors in the absorption of bone, one related to the vascular supply and the other to the bone-forming cells. Persistent vascular dilatation is followed by widening of the canals at the expense of bone, and as the absorption becomes marked the condition of rarefaction, or osteoporosis, occurs. It would appear that in primary vascular resorption the mechanism by which calcium is removed and the canals are widened is a physicochemical one. Any excessive local production of carbon dioxide tends to cause the solution of calcium, for the solubility is directly affected by the carbon-dioxide tension of the blood and tissue fluid. For these reasons only well vascularized living bone can be absorbed quickly. Dead bone is absorbed slowly by osteoclasts.

There are two requisites for ossification: (1) an adequate blood supply, and (2) an adequate supply of calcium. Emphasis is placed upon the importance of circulatory disturbance in modifying the structure of bone. Hyperemia is followed by decalcification and osteoporosis, lessened circulation, and loss of blood supply by necrosis. Repair of bone is carried out entirely by the osteoblasts which line the deep layer of the periosteum, the endosteum, and the haversian canals. The essential function of the periosteum is to supply the outer part of the bone with blood. Removal or separation of the periosteum is apt to be followed by death of the underlying part of the bone.

More recently the literature has contained reports of injuries to bone, especially the neck of the femur in patients treated for cancer of the cervix uteri, as described in 1936 by Dalby, Jacox, and Miller. In a more recent report, Paul and Pohle have described irradiation osteitis following postoperative prophylactic irradiation for cancer of the breast.

In 1933 and 1934, when the authors' first patients with cancer of the breast were treated by interstitial irradiation, it was thought that adult bone was so radioresistant that the therapeutic dose employed would have no deleterious effect upon the ribs. Since that time experience has demonstrated that bone is not so radioresistant as was formerly thought and that permanent damage can result from a therapeutic dose applied to a nearby neoplasm. The authors have been unable to find any report of rib fractures attributable to gamma irradiation. Pack states that he has seen rib fractures following interstitial radiation therapy of mammary cancer.

The authors presented 10 patients who were treated with gamma irradiation for cancer of the breast and who subsequently developed fractures of the ribs. These patients were free of clinical evidence of local or metastatic disease. In most instances the fractures appeared in less than two years. In their early experience the authors were not in the habit of making roentgenograms of the chest in the absence of symptoms, and consequently many fractures were probably present long before their discovery. In one case a fracture was detected as early as eleven months after treatment.

In the differential diagnosis traumatic fracture and neoplastic invasion must be considered. The authors believe that a traumatic fracture can be ruled out on the basis of a careful history in each instance. In neoplastic invasion the area treated shows regeneration of bone. The lack of progression of destruction and the smoothing off of the ends of the fragments militates against a neoplastic process. Despite histopathological verification, except in one case, the authors believe that the clinical condition of the patient and the lack of evidence of cancer elsewhere justifies the consideration of these rib changes as due to a non-neoplastic post-gamma irradiation effect. They believe that this effect is brought about by an interference with the blood supply of the ribs. It is therefore evident that adult bone is not resistant to irradiation directed to a nearby neoplasm. ROBERT T. MCELVENNY, M.D.

Griesemer, W. D.: Complicated Traumatic Dislocations of the Hip. *Am. J. Surg.*, 1944, 63: 16.

The simple, uncomplicated dislocation of the hip can usually be reduced by one of the methods in general use—Allis, Leadbetter, Bigelow, or Stimson. However, the cases complicated by fractures, either of the femur or of the acetabulum and pelvis, often are difficult to manage.

Attempts to reduce the dislocation should be made as early as possible, and depend on the complicating conditions. The force should be carefully controlled to avoid injury to the soft parts, especially the sciatic nerve. If manipulation is unsuccessful, traction either by the Russell method, which may be sufficient in some cases, or skeletal traction through the femur, should be instituted.

The author believes that skeletal traction is preferable, especially in complicated displacements, since by this method one avoids the possibility of pressure ulcerations following prolonged traction, which occurred in his treatment of one patient. During this period of traction, frequent x-rays should be made to check progress, and further attempts at reduction should be tried when conditions indicate. If these fail, open operation should follow, preferably within three weeks, as operation becomes increasingly difficult. Following reduction, fixation by cast is indicated in the simpler cases. In others, in which there is extensive fracture of the pelvis and acetabulum, skeletal traction should be continued for eight weeks. Active motion of the hip and knee should be encouraged to the degree possible and should be limited by pain. Numerous x-rays are required to follow progress.

The authors believe that all patients should be fitted with a caliper brace to allow walking without

direct stress on the joint, as aseptic necrosis of the head with associated joint changes may follow in a certain number of cases, even if not of a complicated type. These changes are due to the interference with circulation caused by the damage to the ligamentum teres and other structures carrying nutrient circulation. Such disturbances have been known to occur even three to four years after injury. Follow-up care is, therefore, very important, and x-ray studies are necessary at certain intervals for early detection of such changes. With these possibilities, the prognosis must be guarded even in the simpler cases. Detailed reports of 4 cases, including roentgenograms, are presented. ROBERT P. MONTGOMERY, M.D.

ORTHOPEDICS IN GENERAL

Wilson, J. L.: The Prognosis of Poliomyelitis and Treatment of the Commonly Fatal Types. *J. Michigan M. Soc.*, 1943, 42: 955.

In discussing the prognosis of poliomyelitis, two problems must be taken into consideration: the possibility of death and the possibility of paralysis. Mortality figures varying from 5 to 25 per cent are reported. This wide range is due to inclusion and failure of inclusion of definite but mild cases of poliomyelitis. However, it has been found that the mortality rate is apt to be greater in small than in large epidemics.

In a community where the doctors are well aware of the disease, the mortality rate is generally less than 5 per cent and four-fifths of the deaths are due to bulbar involvement, the remainder to paralysis of the intercostal muscles and of the diaphragm.

Bulbar cases are divided into two groups:

One group shows irreparable damage of the "vital centers." Paralysis of the vagus nucleus results in a rapid heart rate with ultimate dilatation of the heart and gross disturbance of the respiration. The vasomotor system is upset. There is very little to be done to alter the ultimate fatal course of this group of cases.

The predominating symptom of the other group of bulbar cases is paralysis of the pharyngeal muscle. The patients cannot swallow nor can they cough. The dangerous effect of the pharyngeal paralysis is that it seriously interferes with inspiration and causes exhaustion of the patient. Serous aspiration is frequent. An attack of choking may lead to anoxia which may change the course of the disease entirely.

These patients must be treated with postural drainage, nothing by mouth, and the gentlest nursing care. In very emotional patients who cannot tolerate mechanical aspiration of the pharyngeal secretion, tracheotomy is justified, and in some instances is life-saving. There is 100 per cent recovery from the pharyngeal paralysis if life can be preserved through the first week of the disease.

The treatment of patients with paralysis of the respiratory muscles consists in the use of the respirator. This is justified in all instances of paralysis of the respiratory muscles. Because the final outcome of the disease is not known in the acute phase, the respirator should be used before respiratory distress is too great.

In an analysis of a number of reported series of cases considerable variation in the ultimate result of the treatment is noticed. This is due to the lack of uniformly recorded accurate and thorough muscle examinations.

Some of the best studies were carried out in New York and Massachusetts where quantitative determinations of the degree of paralysis in 100 separate muscle groups were recorded over a period of from four to five years. A group of patients received convalescent serum in the preparalytic stage. Paralysis occurred in 65 per cent. Later studies confirmed this high figure. Three fourths of these patients showed no important or handicapping paralysis.

It is obvious that a great number of cases of paralysis recover spontaneously over a period of months and even years.

Certain clinical features offer a hint for the prognosis. Spinal-fluid examination offers no help. High fever at the onset very often indicates a bulbar type of poliomyelitis. Severe muscle tenderness often is associated with no paralysis while epidemics in which muscle tenderness is absent are accompanied by severe paralysis. It is sometimes very difficult, especially in children, to differentiate true paralysis and paralysis in an extremity due to pain (pseudoparalysis as found in scurvy, greenstick fractures). The most common form of pseudoparalysis is found in the anterior neck muscles which completely recovers once the pain disappears. Patients with paralysis of the intestines, bladder, pharynx, and palate will recover from it if they live.

GEORGE I. REISS, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Langley, G. F.: Gunshot Wound of the Innominate Artery. *Brit. M. J.*, 1943, 2: 711.

An American rear gunner aged twenty-three, injured in a plane by an enemy cannon-shell fragment at 7:30 in the morning, was admitted to the hospital at 1 p.m. He was conscious but had moments of confusion; he complained of a feeling of pins and needles in his left wrist and hand, which he could not move. A roentgenograph taken through his clothes revealed a cuboidal metal foreign body, 1 cm. in size, behind the right side of the manubrium sterni at the level of the first chondrosternal junction. Cerebral symptoms developed within five hours of the injury, and were ascribed to spasm of the carotid artery with intramural clotting, general anemia, and low blood pressure. The patient's condition deteriorated progressively, and at 8 p.m. operation was performed under intratracheal anesthesia.

At the innominate bifurcation a blue-domed clot was seen on the anterior surface, and it was evident that a puncture had occurred at this site. An exit laceration of the posterior wall of the innominate artery was found just below the bifurcation. Resection of the bifurcation was therefore carried out after double ligatures of thick silk were applied to the innominate, common carotid, and subclavian arteries. Following the operation the blood pressure and pulse rate rose. During the night, pulmonary edema developed, and the patient never regained consciousness. HAROLD C. OCHSNER, M.D.

Mitchell, N., and Angrist, A.: Intracranial Aneurysms—A Report of 36 Cases. *Ann. Int. M.*, 1943, 19: 909.

Thirty-six cases of intracranial aneurysm affecting the cerebral arteries in a total of 3,080 autopsies performed in the Queens General Hospital are presented. Forty-two aneurysms are included, subdivided as follows: "berry" 22, mycotic 11, arteriosclerotic 6, syphilitic 2, traumatic (arteriovenous) 1.

In 7 of the 11 mycotic aneurysms, acute bacterial endocarditis due to the streptococcus viridans provided the septic focus; in 3 it was staphylococcus aureus-hemolyticus sepsis; and in the last case it was influenzal meningitis.

The most common sites of aneurysms on the various branches of the circle of Willis were the middle cerebral artery (10 cases), anterior communicating artery (8 cases), anterior cerebral artery (6 cases), internal carotid artery (5 cases), and the convexity (5 cases).

In the mechanism of rupture the presence of arteriosclerosis and of necrosis in the wall of the aneurysm is stressed.

For the further elucidation of this problem it is pointed out by the authors that careful histological study of all ruptured and unruptured aneurysms is indicated for evidence of atherosclerosis, of active degeneration and necrosis, and of specific and nonspecific inflammation. WALTER H. NADLER, M.D.

Pearce, M. B.: Varicose Veins. *Surgery*, 1943, 14: 901.

The author notes that in the management of varicose veins, ligation and injection at the fossa ovalis in the usual manner results in incomplete thrombosis and large thrombi. Recurrences appear in many cases. He presents a new compression-bandage technique, with the ligation of all the branches of the saphenous vein and of the saphenous vein itself at the fossa ovalis, together with low ligation and injection of the saphenous vein only at the low level.

Anatomically there are 3 systems of veins in the thigh and leg: (1) the internal or long saphenous, (2) the external or short saphenous, and (3) the femoral or deep venous system. In reference to varicosities, there is a fourth group which cannot be ignored, called the subcutaneous veins, made up of segmental veins which may communicate with the long saphenous system at different points, or may communicate in segmental fashion between the superficial branches of the long and short saphenous systems. Upon complete obliteration of the circulation in the long and short saphenous systems of the patient with varicose veins, these segmental subcutaneous channels with their varicosities may persist.

These segmental subcutaneous varicose veins are most amenable to injection treatment alone. Injections of sclerosing fluid into the varicosities of either the long saphenous or short saphenous system, without ligation, are almost sure to result in poor response or complete failure.

Mild varicosities of the internal or external saphenous system per se need no treatment and cause no symptoms. Mild varicosities of the subcutaneous group may produce sensations of prickling, discoloration, and even pain. Injection alone will secure results in this small group, but will not eradicate the varicosities of the internal and external saphenous system. Varicosities that are large and tortuous should be treated by active surgical and injection procedures.

The operative procedure used, which sustained excellent primary results and produced no untoward effects, is described.

In conclusion, the author notes that all cases involving the long saphenous vein are treated by uniform ligation of all its branches, and of the saphenous vein itself at the fossa ovalis, without injection of sclerosing fluid into the thigh, together with ligation and injection of the internal saphenous at the lower thigh.

Complete emptying of the veins by compression bandages of the ace or rubber type is a distinct ad-

vantage in reducing the size of the thrombi, and insures better diffusion of the sclerosing fluid into the most distal ramifications of the varicosities.

Five cubic centimeters of sodium morrhuate produce excellent thrombosis in varicosities of the lower leg and this is the maximum amount used in any single vein. It would appear that this technique yields complete obliteration of all varicosities without untoward manifestations. No recurrences are noted. HERBERT F. THURSTON, M.D.

Morton, C. B., Shearburn, E. W., and Burger, R. E.: Synthetic Vitamin K and the Thrombosis of Veins Following Injury. *Surgery*, 1943, 14: 915.

The authors note that vitamin K is used to a great extent in certain surgical patients to combat a bleeding tendency, and in parturient women to prevent hemorrhagic disease of the newborn. Both surgical patients and parturient women are particularly susceptible to thrombosis and thrombophlebitis, although the use of vitamin K does not appear clinically to increase their susceptibility. A study is made of a group of patients, and of a series of experiments with animals to determine what influence, if any, the use of vitamin K might have on thrombus formation.

A lowered blood prothrombin with its bleeding accompaniment has been observed in hemorrhagic disease of the newborn, obstructive jaundice, severe liver damage, and in chronic gastrointestinal diseases and conditions such as sprue, chronic ulcerative colitis, intestinal polyposis, and gastrocolic fistula. The attendant hemorrhages have been treated prophylactically and therapeutically in the last few years with vitamin K, and by the addition of bile salts in the jaundiced patient.

Waddell, Guerry, and Birdsong made a study of prothrombin deficiency in infants in the hospital. Hemorrhages in the newborn were obviated by the administration of vitamin K concentrate, and synthetic vitamin K was given to infants in the first few days of life, and to mothers in the last two weeks of pregnancy. No observer so far has reported an increased incidence of thrombosis or thrombophlebitis in patients treated with vitamin K.

Clinically, vitamin K has proved efficacious in the prophylactic and therapeutic treatment of hemorrhagic diathesis of the newly born infant, with no increase in the incidence of thrombosis. The incidence of thrombophlebitis in only 1 of 700 pregnant women given vitamin K in its various forms, orally and intravenously (as prophylaxis against hemorrhagic disease in the infant), was 0.14 per cent over a period of two years. In a preceding ten-year period, thrombophlebitis occurred in 28 of 5,728 women who had been delivered but had not been given vitamin K, an incidence of 0.48 per cent. As has been shown by Norris and Bennett, the average value of plasma prothrombin in mothers at delivery (111 per cent) is greater than that in normal controls. This may contribute to the slightly increased incidence of thrombophlebitis in parturient women.

A number of experiments on dogs were carried out with a view to determining the possible influence of vitamin K on thrombus formation. The radial and saphenous veins of the legs of 52 dogs were traumatized mechanically by scarifying the intima with a hooked needle. The veins were then removed at forty-eight and ninety-six-hour intervals. Twenty-seven of the animals received a surplus of synthetic vitamin K along with the regular diet for a week prior to the injury, and the remaining 25 animals were utilized as controls. Prothrombin times, hematocrit determinations, and clotting times were ascertained in each animal at intervals, but no effect of the synthetic vitamin K administration was observed.

The incidence of thrombosis after injury to the intima of the veins was not significantly increased coincident with the administration of synthetic vitamin K, this being 33.0 per cent in the control group and 38.0 per cent in the group receiving vitamin K. The prothrombin values, which are important in the coagulation process, did not change significantly after the administration of synthetic vitamin K. Dogs with a hematocrit reading below 40 per cent revealed a slightly higher incidence of thrombosis in both the control and the vitamin-K-fed group.

In conclusion, the authors note that the clinical and experimental data reported demonstrate that an excess of vitamin K does not result in an increased rate of thrombosis. HERBERT F. THURSTON, M.D.

BLOOD; TRANSFUSION

Gray, S.: The Use of Fibrinogen in a Rapid Method of Determining Cell Volume. *Am. J. M. Sc.*, 1944, 207: 29.

The determination of the volume of packed red cells has assumed an increasingly important role both in the differential diagnosis of the anemias and in the evaluation of blood volume, shock, hemorrhage, and dehydration. The method in common use, however, has been unreasonably long and time-consuming. It has been observed that the addition of electrophoretically pure fibrinogen to heparinized blood increased the sedimentation rate enormously, the increase being proportional to the amount of fibrinogen added. When 0.4 gm. per 100 cc. of fibrinogen was added to whole blood, the cells settled so rapidly that they approached cell volume at the end of one hour. Since the rate of settling is proportional to the size of the cell aggregates, and since the size of the cell aggregates depends upon the amount of fibrinogen added to the plasma, the use of fibrinogen in developing a rapid method for determining cell volume was investigated.

Centrifugation for five minutes of heparinized blood containing an electrophoretically pure bovine fibrinogen solution yielded cell volume determinations which were accurate to within 0.5 per cent of the cell volumes of unaltered blood centifuged for sixty minutes at 1,800 r.p.m. The accuracy of the five-minute method was within the range of accuracy

of present methods requiring from thirty to ninety minutes of centrifugation.

This rapid method of determining cell volume was applied to 50 patients and was found exceedingly accurate within a wide range of cell volumes (17 to 68 per cent) and sedimentation rates (0.5 to 42 mm.). The mean deviation was 0.24 per cent, and the accuracy of the method was not affected by the range of cell volume or sedimentation rate.

Comparative five-minute cell-volume determinations of blood containing added fibrinogen, homologous plasma, and saline solution indicated that accurate and consistent results were obtained only in the blood specimens containing the added fibrinogen solution.

The most accurate results were obtained by centrifugation of the blood containing the fibrinogen solution for five minutes at from 1,500 to 1,800 r.p.m.

When heparinized blood was subjected to consecutive five-minute periods of centrifugation and the level of the red blood cells was recorded graphically the resulting figure was a vertical curve consisting of two phases: rapid settling and packing. The addition of the fibrinogen solution to blood increased the rate of settling of the erythrocytes and produced a more vertical curve so that the first phase was completed in five minutes, and recorded the cell volume.

STEPHEN A. ZIEMAN, M.D.

Loutit, J. F., and Mollison, P. L.: Disodium-Citrate-Glucose Mixture as a Blood Preservative. *Brit. M. J.*, 1943, 2: 744.

In assessing the preservative value of certain citric-acid-sodium-citrate-glucose mixtures as preservatives for stored blood, it was found that a mixture of 100 cc. of 2 per cent disodium citrate with 20 cc. of 15 per cent glucose added to approximately 430 cc. of blood had two advantages over the standard trisodium-citrate-glucose mixture as an anticoagulant and preservative solution for blood storage: (1) its preservative power, judged by the survival in vivo of erythrocytes stored in the solution, is considerably superior; and (2) the mixture can be autoclaved without the production of any caramel.

The only disadvantage of this disodium citrate solution is its liability to permit clot formation if the blood is not carefully mixed with the solution when it is taken. This is because the mixture contains less citrate radical than the standard trisodium-citrate solution. STEPHEN A. ZIEMAN, M.D.

Jensen, H. L.: The Use of Sulfonamides for Suppression of Bacterial Growth in Stored Blood. *Med. J. Australia*, 1943, 2: 376.

When human blood is collected on a large scale for transfusion purposes, the danger of occasional contamination with micro-organisms from extraneous sources, as well as the possibility of bacteriemia in the donors, can never be altogether eliminated. If the contaminating bacteria or other organisms are able to grow in blood kept at low temperature, they may, even if nonpathogenic, cause harmful changes, such as hemolysis or the production of pyrogenic substances, during the storage of the blood. The addition of some bactericidal or bacteriostatic agent to the blood has decided advantages.

Since mercurial antiseptics are almost useless as preservatives in whole blood, and rivanol causes hemolysis, attention was directed to sulfanilamide and sodium sulfathiazole in concentrations of from 0.05 to 0.2 per cent. It was found that these substances have strong bacteriostatic effects.

The following bacteria were tested for ability to grow in refrigerated blood containing the various bacteriostatic agents: (1) bacterium S, a non-spore-forming, Gram-negative, actively motile rod which produces a whitish growth on agar; (2) bacterium R.I, a non-spore-forming, Gram-negative, nonmotile rod which produces a slimy growth on agar (light yellow at 5° C. and pale greenish at 30° C.); this was isolated from soil kept at 5° C.; (3) bacterium B, a non-spore-forming, Gram-negative, nonmotile rod which produces an ochre-yellow growth on agar; this was isolated from blood exposed to contamination at 5° C.; (4) corynebacterium R.IV, a non-spore-forming, Gram-positive, nonmotile rod of irregular cell shape, which produces a white growth on agar; this was isolated from soil kept at 5° C.; and (5) pseudomonas fluorescens.

All these bacteria grew vigorously in broth at 5° C.; the first three grew also in blood, in which they sooner or later produced a dark purplish (eventually almost black) color. It was seen that some bacteria can multiply quite strongly in the presence of a 0.05 per cent concentration of sulfanilamide, but they were almost completely suppressed by the same concentration of sulfathiazole. Certain fungi are more resistant to sulfonamides and seem to represent dangerous potential contaminants.

The addition of a 0.05 per cent concentration of sodium sulfathiazole to the blood would therefore seem to be a valuable safeguard against deterioration during storage, provided that the blood is only lightly contaminated. STEPHEN A. ZIEMAN, M.D.

Slagle, T. D., and Pons, J. A.: Reciprocal Transfusions of Blood in Anuria: Report of a Case. *J. Urol.*, Balt., 1943, 50: 503.

The clinical trial of a reciprocal transfusion of blood in a patient suffering from mercury poisoning and attendant anuria is presented, with complete laboratory studies and observations. Gradual exsanguination of a patient and replacement with blood drawn from healthy donors is reported and cited in several instances by the authors. However, this usually entails an unlimited supply of donors. Reasoning that the organs of a healthy person function at only a small percentage of their capacity and that they might well take care of a patient's blood affected by the temporary failure of any one of several organs during the period of dysfunction, the authors undertook the present study.

It was thought that when there is no danger to the donor, most healthy individuals would be willing to

let some organ of the body perform temporarily its function at above normal requirements if this were the means of saving the life of some loved one or friend. The authors pose the question: Would he not, after all, have less inconvenience from the exchange of a quart of blood than from the loss of one-half that amount in the average transfusion?

The patient involved in the present reciprocal transfusion was a forty-year-old male who manifested acute signs and symptoms of mercury poisoning following overdosage of mercury succinamide, 1/32 gr. having been taken daily for several months, and a single dose of 1/8 gr. having been taken just prior to the onset of the present illness. The plan was explained to, and understood by, both donor and patient. Their bloods proved to be of the same group and compatible. Blood was taken for chemical analyses from both. A liter of blood was withdrawn from each and immediately citrated, and the blood from the donor was given to the patient and that from the patient was given to the donor. Several minutes after the transfusion was completed a few cubic centimeters were allowed to run out through each needle and blood samples were obtained for chemical analysis.

Although isotonic saline and glucose solution was given in large amounts during the first forty-eight hours of hospitalization, and in spite of hot pack and sedation, the patient remained anuric and his condition grew worse. At this point, reciprocal transfusion was started. The patient received 1,000 cc. of blood in this manner on the third day of his illness, two transfusions on the fourth day, and one each on two successive days. Thus, five reciprocal transfusions were carried out in the course of four days.

The patient became mentally clear after the first transfusion and remained so thereafter. Nausea and diarrhea subsided, and following the fourth transfusion, after nine-and-one-half days of anuria, the patient voided 18 cc. of urine. The urinary output gradually increased to almost 1,400 cc. There were frequent headaches, and on the eighteenth day the patient complained of sudden unbearable occipital headache, radiating down the spine, which was followed by convulsion and death.

Death was attributed to intracranial hemorrhage. The pathologist believed that, although no frank point of rupture was identified, it seemed likely that such did occur in one of the vertebral arteries secondary to necrosis and hemorrhage into its wall, inasmuch as such lesions without rupture were noticed in areas of the right vertebral artery and in the right renal artery. The cause of these lesions was not clear but might have been the mercury poisoning per se or the subsequent uremia and hypertension.

A tabulation of the blood-chemistry studies, including nonprotein nitrogen, urea nitrogen, uric acid, creatinine, and chloride determinations, showed some reduction in the case of the patient and no appreciable changes as far as the donor was concerned. Other than the development of a slight fever to 102°F. with associated symptoms of upper respiratory infection after two transfusions in one day, the donor had no untoward reactions. It was believed that even this transient fever was not related to the transfusions, but only at the donor's insistence was the experiment continued.

The authors believe that a single case such as this does not allow of any definite deductions. The re-establishment of renal function cannot be attributed to the transfusions since patients with mercury nephrosis have recovered without them and with even longer periods of anuria. Likewise, the intracranial hemorrhage cannot be attributed to the transfusions. There was no way of determining the extent to which the exchange of blood kept the retention of nitrogenous waste substances from rising to lethal levels. The impression was that prompt clinical improvement occurred.

While the transfusions were stopped after four days, the authors saw no reason why the treatment could not have been continued for much longer if considered necessary. There was no deleterious effect on the donor as judged from blood chemical analyses. The experiment, they conclude, was done not only for its theoretical implications but also because of its possible therapeutic value and its practicability when and where unlimited supply of blood donors is not available.

ARTHUR H. MILBERT, M.D.

Munro, F. L., and Jones, H. W.: The Detrimental Effect of Frequent Transfusions in the Treatment of a Patient with Hemophilia. *Am. J. M. Soc.*, 1943, 206: 710.

Clinical and laboratory observations were made over a period of three years on a hemophiliac thirty-six years of age, who received a total of 24 blood transfusions, of which 6 were of whole blood and 18 of plasma. Some of these transfusions were given with prophylactic intent.

After a brief beneficial period it was noted that the transfusions no longer affected the clotting time of the patient's blood. It was found that the hemophilic plasma developed the property of retarding the coagulation time of normal plasma. This was believed to be due to the presence of an inhibitory constituent, antithromboplastin, which increased in concentration as the result of repeated blood transfusions. The abnormal rise and accumulation of antithromboplastin was associated with an aggravation of clinical symptoms in this hemophiliac.

The author suggested that it would be better clinical judgment to reserve the transfusions of blood for only the acute manifestations of hemophilia.

BENJAMIN G. P. SHAFIROFF, M.D.

Litwins, J.: Universal O Blood Transfusion: Combination of Pooled Plasma and O Cells. *J. Am. M. Ass.*, 1943, 123: 630.

Litwins believes that the combination of o cells with pooled plasma is a safe and economical medium

of universal blood transfusion. The pooling diminishes the titer of the isoagglutinins mainly by dilution and through neutralization of the isoagglutinins by group substances in solution. In this way, too, there is no waste of red cells since they are used in pooled plasma. FREDERIC W. ILFELD, M.D.

State, D., and Levine, M.: Human Plasma and Serum Toxicity. *J. Lab. Clin. M.*, 1943, 28: 1786.

The authors note that reactions have been reported for both serum and plasma following their intravenous administration in human beings and animals. Serum is suspected of causing more reactions than plasma, but some workers prefer serum for other considerations, and they either deny that reactions occur, or are of the opinion that the reactions are not important. It is probably correct to conclude that reactions occur with both serum and plasma. As to serum, early experimentation may explain part of its excessive toxicity.

Patients sensitive to the A or B plasma by skin tests with repeated A or B plasmas and some AB plasmas are also sensitive by skin test to the purified substance. These patients are also sensitive to group A or B plasma or AB plasma administered by the intravenous route. They have reactions following the intravenous administration of the purified A and B substances. As control measures, all plasmas are tested for sterility. Some have been divided into two parts, part going to a sensitive individual with a resulting reaction and part to a nonsensitive individual of the same blood group without a reaction. Individuals sensitive to one group-specific substance do not necessarily show sensitivity to the other group-specific substance, although there was one instance in which the patient was sensitive to both.

Patients displaying sensitivity do not necessarily have an allergic history. There does not seem to be any correlation between the amount of antibody present in the recipient and his sensitivity to the factors. However, only those individuals who are in the blood group in which the specific antibody is found corresponding to the specific A or B substance show sensitivity. Not all individuals show this sensitivity even if they have the antibody.

The severity of any reaction depends upon the reacting material and on the condition of the patient. A reaction which would not disturb a normal individual might kill a patient in a precarious condition. A case is presented which indicates that reactions occur under anesthesia and that they may be serious if unrecognized.

Patients sensitive to a single factor may not show as marked a reaction to pooled plasma or serum because of the dilution of the A and B substances. When the patient is sensitive to both factors, dilution would play less of a role. Neutralization of the A and B factors does not occur in pooled specimens of plasma or serum; hence, pooling is not a sure method of preventing reactions due to these substances.

Reactions may occur because of factors other than the A and B substances. The following may be the cause of reactions when the A and B substances are not involved: (1) the presence of allergens in the plasma or serum; (2) the presence of reagins in the plasma or serum; (3) the presence of pyrogens; and (4) the presence of immunological factors as yet unknown. Cases observed which are due to factors other than the A and B substances are presented.

The skin test is more likely to be positive when associated with an allergic reaction than with a pyrogenic type of reaction.

In conclusion, the authors note that they have presented important transfusion reactions due to the A and B factors in both plasma and serum and also reactions due to factors in plasma other than the A and B substances. The skin test with the plasma is a good method of indicating sensitivity to the plasma in many of the cases and an aid in preventing transfusion reactions.

HERBERT F. THURSTON, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Schorstein, J.: Gunshot Wounds of the Fronto-Orbital Region. *Lancet*, Lond., 1944, 246: 44.

The author reports 10 cases of gunshot wounds of the fronto-orbital region with tears of the dura, brain injury, and cranial intercommunication with the upper respiratory tract. The injuries comprised 4 per cent of all the penetrating head injuries admitted to this forward head center near the front lines.

The primary surgical principles recommended for the treatment of fronto-orbital injuries are complete surgical exploration and débridement, aspiration of pulped brain tissue, removal of orbital bone splinters, and control of hemorrhage. The walls of the involved sinuses should be opened and the mucous membrane which is a potent source of infection should be scraped away. The resultant débrided area leaves a clean cavity which must be sealed by direct closure of the wound in two layers. If it is not possible to close the dura a fascia-lata graft should be taken. The skin wound should be closed separately.

This method applies only to brain injuries because of the fact that sepsis rarely follows primary closure. Although the grafting of fascia lata for dural closure is ideal, the operating time is so unduly prolonged in some cases that the cavity must be left open and packed with soft paraffin gauze. In the latter group all dead space should be obliterated, and the brain and sinus spaces should be packed individually. The dressings are then fixed with plaster-of-Paris skull caps.

Other important considerations involve endotracheal anesthesia and complete preoperative x-ray studies. BENJAMIN G. P. SHAFIROFF, M.D.

Holman, E.: Experiences with Chest Wounds from the Pacific Combat Area. *Ann. Surg.*, 1944, 119: 1.

Transportation, treatment, and convalescence of the patient with wounds of the chest provide unique and difficult problems. The obvious vulnerability of the chest, the fatal potentialities of large sucking wounds, and the quick fatality in injuries to the heart and large vessels are all reflected in the high mortality, estimated at approximately 40 per cent.

Conservatism in thoracic injuries seems to be the routine treatment advocated by British and American surgeons. Among 2,500 battle casualties, not a single operation was performed primarily to deal with a wound of the chest. The removal of foreign bodies was delayed until the patients reached a base hospital. Aspiration was employed only to relieve mediastinal shift or respiratory difficulty. Empyema developed in only 3 of 63 penetrating wounds of the chest.

This is in contrast to the radical exploration championed by some civilian and military authorities.

Holman narrates case histories demonstrating his experiences in the Pacific Combat Area with patients having chest wounds and setting down what he considers the proper surgical management.

There were in this series 36 cases of gunshot wounds of the chest, 29 of which showed marked dyspnea, 16 hemoptysis, 19 hemothorax (12 of which were aspirated for a total of 27 times). Three cases subjected to aspiration were given air for replacement; 2 of these were complicated by empyema. Seven cases of hemothorax were not aspirated, and uncomplicated recovery took place. Eight cases had retained foreign bodies, which were removed in 5 cases; 8 cases presented fractured ribs, for which no particular treatment was necessary; 6 had sucking wounds, requiring early closure; and 6 were complicated by empyema, which will require a thoracoplasty for cure in 2. There were no deaths.

The following treatment was given these patients:

Clean-cut bullet wounds without symptoms required simple dressing only, whereas jagged dirty wounds of entrance and exit were excised immediately, when possible, or filled with sulfonamide powder and excised later when the opportunity presented, if the wound was still free of pus.

Large sucking wounds of the chest were closed at the time of injury; if operative closure was not immediately possible, the wound or defect was covered with a sterile rubber glove or was filled with sterile vaselined gauze, covered with a voluminous dressing and fixed in place with a large adhesive bandage encircling the chest. This produces fixation of the mediastinum which will permit the thoracoplasty that may be necessary later to close the defect.

Immediate operative measures consisted of semilunar, relaxing incisions in the muscle layers either on one or both sides of the defect which permitted closure of the muscles without tension. Semilunar, relaxing incisions in the skin on one or both sides of the defect may permit closure of the defect. The resulting raw surfaces, not including the defect, were later skin-grafted. Resection of one or two ribs on one or both sides of the defect permitted sufficient mobilization of the soft parts to bring the tissues together without tension.

The sulfonamides were used liberally, both locally and orally in all instances. In a case of gross contamination of the pleural cavity by dirt or clothing, drainage was done with an airtight catheter introduced through an intercostal space well separated from the closed wound.

Hemothorax was a frequent complication of gunshot wounds but surprisingly often was not infected; it may be resorbed at times. Aspiration was limited to cases showing respiratory embarrassment, to cases suspected of harboring a complicating infection, and to cases in which blood or fluids failed to resorb after two or three weeks.

A hemothorax or serosanguinous effusion that persisted beyond two or three weeks without diminution could be aspirated without replacement with air.

The author contends that wounds of the lungs do not require operative intervention per se unless uncontrollable hemothorax or uncontrollable tension pneumothorax demand it, and the removal of foreign bodies in the chest may be safely postponed in most instances until favorable conditions prevail.

Traumatic lesions of the chest including lacerations of the lung require a prolonged convalescence and a return to service duty should be postponed until roentgenographic evidence of intrapulmonary damage has largely disappeared and is minimal.

STEPHEN A. ZIEMAN, M.D.

Wise, R. A., and Romansky, M. J.: Massive Resection of the Jejunum and Ileum for Gunshot Wounds of the Small Intestine and Its Mesentery. *J. Am. M. Ass.*, 1943, 123: 896.

Resection is frequently indicated in the treatment of penetrating wounds of the small intestine and its mesentery. Wounds which have destroyed a section of the bowel, impaired its blood supply by injury to its mesentery, or caused large contiguous lacerations cannot be closed; they require resection. The portions requiring resection may be multiple, involving various segments of the intestine, with normal bowel between them. It is important to determine whether a single resection of the multiple wounds can be performed, or whether multiple resections of the involved segments should be undertaken. Multiple resections definitely increase the mortality. If a single resection of the involved bowel is decided upon, it may be necessary to remove an extremely long section. Thirty-three per cent of the small bowel can be removed without nutritional disturbance, 50 per cent being the limit.

In a case of multiple gunshot wounds of the small intestine and its mesentery requiring resection, normal metabolic function was maintained following the resection of 8 ft. of jejunum and ileum. If resection is indicated, a single resection rather than multiple resections should be performed for lesions lying within an 8-foot segment of intestine. The treatment of the associated hemorrhage is important.

SAMUEL KAHN, M.D.

OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

Brambel, C. E., and Loker, F. F.: Application of Dicoumarin (3, 3'-Methylene-Bis-[4-Hydroxycoumarin]) in Trauma and Gangrene. *Arch. Surg.*, 1944, 48: 1.

Dicoumarin, the active biological principle of spoiled sweet clover which causes the hemorrhagic disease in cattle, exerts no anticoagulant properties on blood directly but produces its effect through some organic tissue of the body. In the authors' experience the therapeutic impairment of the coagulation mechanism by chemical agents has proved decidedly advantageous in cases of trauma and of various types of gangrene. Vascular failure resulting in thrombosis and gangrene has been found to be controllable by in-vivo anticoagulants. Such surgical applications of these chemical agents should prove of inestimable value during the present national emergency when industrial accidents, war wounds, and other conditions incident to war, such as trench and immersion foot, are so prevalent.

The authors studied the efficacy of in-vivo blood anticoagulants, namely dicoumarin and heparin, in a series of cases involving various types of gangrene and trauma, classified as follows: (a) post-traumatic conditions with associated gangrene following crush injury; (b) diabetic and arteriosclerotic gangrene; (c) frostbite.

In trauma and gangrene the following conditions are manifest: (1) conditions favoring thrombus formation; (a) injury to the endothelial lining of the blood vessels, (b) accelerated prothrombin clotting time (detectable in dilute plasma), and (c) liberation of excess thromboplastin (thrombokinase) by traumatized tissue; and (2) marked swelling which interferes with normal circulation and the oxygenation of the tissues. By means of in-vivo anticoagulants the enhanced prothrombin clotting mechanism can be disrupted for any desired period without deleterious effects in the patient. In this manner proper physiological circulation can be maintained until natural processes supervene.

Strong indications have been obtained that prevention of the extension of already well established gangrene and prevention of the development of gangrene in post-traumatic cases can be accomplished. Without exception, all cases exhibited increased prothrombin activity, detectable in dilute plasma. This finding suggests an indication for the administration of hemorrhagic compounds to alter biochemical conditions favoring thrombus formation.

The use of in-vivo anticoagulants (dicoumarin) in the treatment of patients with granulating and ulcerative lesions is not contraindicated if caution and adequate control are exercised. In this connection, too, much emphasis cannot be placed on the value of frequent determinations of the prothrombin clotting time as an index to dosage. No set dosage for dicoumarin was found for the patients in the series of cases presented. In some the clotting mechanism was found to be refractive, and therefore they required much larger doses than others.

No contraindications were found when sulfonamide compounds and dicoumarin were used concomitantly if average normal renal and hepatic function were present. No evidence of hepatic damage following long periods of oral administration of hemorrhagic compound was demonstrable by any available test.

One patient was treated by amputation below the knee since it was feared that he could not withstand the shock of midthigh amputation. This one instance suggests that the time-honored procedure of

midthigh amputation in a patient with arteriosclerotic and diabetic gangrene of the toes may be supplanted by amputation at a site of election below the knee if dicoumarin is administered.

JOSEPH K. NARAT, M.D.

Sano, M. E., Holland, C. A., and Babcock, W. W.: The Use of the Coagulum-Contact Method in Surgery. *Surg. Clin. N. America*, 1943, p. 1673.

The coagulum-contact method is a physiological means for the firm application of skin grafts to the recipient base and for the furtherance of adhesion between cut surfaces. Two solutions are prepared from the patient's blood which is centrifuged. The amount of blood withdrawn is usually 5 cc., and autogenous preparations are best. Solution A is the heparinized blood plasma dissolved in Tyrode's solution, a buffered salt solution containing glucose. In solution B is contained the layer of white cells, obtained also from the centrifuged mass. The cells are suspended in Tyrode's solution and are broken down by vigorous shaking of the tube. In addition to the adhesive properties of this mixture, the leucocytic extract has growth-promoting properties and therefore wound healing is effected more rapidly than normal. Solution A, the plasma solution, is painted over one of the surfaces, and solution B over the other surface. The use of a camel's hair brush is best for this purpose. On apposition or contact of the two surfaces, an adhesive coagulum is formed. This medium has been used for the fixation of skin grafts, for lacerated wounds of the skin, and for wounds of the liver and spleen. It may be used also on muscle grafts for the control of capillary hemorrhage.

BENJAMIN G. P. SHAFIROFF, M.D.

Lamont, E. S.: Reconstructive Plastic Surgery of the Absent Ear with Necrocartilage: An Original Method. *Arch. Surg.*, 1944, 48: 53.

The individuality of the ear cartilage, and its position away from the head, makes reconstruction of the absent ear one of the most complex of all plastic problems. The ear is partially or totally absent in approximately 1 of 20,000 infants at birth. The reconstruction of the absent auricle may physiologically be begun when the patient is five or six years old, as at this time the ears have virtually gained their full normal growth.

Partial absence of an ear suggests several methods of reconstruction, depending on the location of the missing part. Should the defect be of the helix, a small delayed flap, borrowed from the mastoid tip, with its base at the margin of the defect may be folded on itself. The resultant raw surface on the mastoid area may then be covered with a thick split-skin graft. Reconstruction of the ear lobule may be carried out with a rectangular delayed flap from the neck, raised to the ear in one stage, then later severed from its base; it should be long enough to leave it sufficiently long so that it may be folded on the posterior aspect. The resulting defect on the neck may be undermined and sutured in a straight line. When the tragus is absent a delayed flap from the face, with its base posterior, is turned on itself, and the resultant raw surface is grafted. Whenever framework is necessary, struts of preserved cartilage or necrocartilage may be used. On occasion, odd cases are reported in the literature concerning the resuturing of a totally or partially absent ear that has been severed and dropped to the ground. Obviously this is an impossibility. Also, ears or portions of ears cannot be taken from one person and transferred to another. The prosthetic ear has a definite place as a temporary procedure. However, as a rule, the patient would rather have a surgically constructed one, even though it is not perfect, as long as it is made of tissue attached to his body.

In surgical reconstruction of the totally absent ear, careful photographic studies are made of the patient's head, which include the good ear and the affected one for comparison. Though it may be impossible to reproduce a replica of the good ear, the surgeon must attempt to obtain one of the same size and contour. A plaster cast is made of both ears; they are studied and compared. The model of the affected ear is then built up with clay, so as to gage the ear necrocartilage required.

In the first stage a curved incision about 1½ in. long is made on the posterior aspect of the mastoid area. The blade is carried through to just above the superficial fascia. Through the elliptic incision the skin is carefully undermined and a pocket is created that will house the future ear cartilage. The flap is made as thin as possible and yet thick enough to carry circulation for its latent chore. Thinness is desired so that the flap may drape itself well into the convolutions peculiar to the ear cartilage, in this case, ear necrocartilage. Bleeding is controlled, the flap is allowed to return to its bed, and the incision is sutured. This may be repeated in order to obtain as thin a flap as possible, so that the skin may envelop itself into the interstices of the whorls of the ear necrocartilage.

In the second stage the ear necrocartilage has been previously prepared by meticulous removal of the tissue and perichondrium. A dozen small holes have been made in the body of the cartilage to allow the granulation tissue to rivet through and hold it in place when implanted. The thin delayed flap over the mastoid area is raised again, bleeding is carefully controlled, and the ear necrocartilage is placed in its previously prepared pocket. Cotton saturated with alcohol and small pieces of marine sponge are used to tuck the skin into the convolutions of cartilage. Sulfanilamide crystals are thinly spread into the pocket, both to avoid infection and possibly to help create fibrosis. A clavicular tubed pedicle is started at this time. Its dimensions are such that it may be waltzed up the neck to the ear area. It is made some 4½ in. long and 1¼ in. wide. Neck tubes are avoided when possible so that no disfiguring scars remain. The tubed pedicle is severed from its anterior connection in three or four weeks and waltzed to a trap door on the neck. In another three or four weeks it is

brought to the base of the ear; in another month to the position of a new helix.

In the third stage an incision is now made ¼ in. above the necrocartilage at its periphery and carried from the anterosuperior aspect of the ear some 3 in. around posteriorly down to the fascia. The tubed pedicle is opened and allowed to inhabit itself within the incision. Laterally, slightly away from the head, the tube is fashioned to simulate a helix, while behind the ear necrocartilage now serves as a thick covering. LOUIS T. BYARS, M.D.

Aufricht, G.: Evaluation of Pedicled Flaps Versus Skin Grafts in Reconstruction of Surface Defects and Scar Contractures of the Chin, Cheeks, and Neck. *Surgery*, 1944, 15: 75.

The treatment of skin defects constitutes an important phase of plastic surgery. In general, it can be stated that regardless of the cause, the principles of reconstruction are the same. The issue of first importance in granulating wounds is quick epithelization, and the most important treatment is early skin grafting. The treatment of old scars offers an entirely different problem. Extensive burn scars, when the scars have been caused by second-degree burns, and when the scars are soft, superficial, and smooth, offer a real dilemma. It may be wise to advise against surgery in these cases, or to do a Z-plastic if a few contracting, scarry bands are present. The same treatment may be used for mild x-ray burns with discoloration.

In the severe scars from burns, or whatever cause, surgical procedures must be employed. There is seldom a choice of an open flap as opposed to a closed or tubed flap. The flap may be formed on almost any part of the body, though the most advantageous sites are: (a) axilloabdominal, (b) transverse or oblique abdominal (transferred usually via hand), and in case of necessity (c) acromiopectoral, and (d) dorsal. In selecting the donor site the following points must be considered:

a. The skin of the donor site must be a good esthetic match in color, texture, and thickness.

b. An adequate amount of skin must be obtainable.

c. It should be relatively convenient to transfer.

d. The secondary scar of the donor area must be hidden, and should not cause functional disturbance.

The following points relative to the forming of the tube are important: (a) strict surgical asepsis, (b) thorough hemostasis within the tube to prevent the formation of hematomas, (c) the length of the flap should not exceed three times the width, preferably not more than two and one-half times (longer tubes should be prepared in sections with intermediate pedicles or in different operative stages), (d) the tube should be formed in the direction of the blood supply, (e) on thin persons the flap should include the entire layer of fat down to the fascia, (f) on fat persons enough fat should be left so that the tube may be filled without causing too much pressure, (g) the tube should be guarded against twisting, (h) the longer the tube, the slower the transfer should be, (i) a tube made of basic proportions can be moved in three or four weeks, and (j) penetrating defects should be lined with a skin graft or flap before the tube graft is transferred.

In reference to good cosmetic results with skin tubes, the following points should be observed:

1. The size of the defect must be carefully observed and the flap should be prepared as wide as necessary since it is impossible to stretch the skin with a good cosmetic result.

2. Large transplants give a better cosmetic result than small ones.

3. No old scar should be spared between healthy tissue and the graft.

4. The replacement should cover esthetic units. If the scar reaches nearly to the nasolabial fold, the transplant should extend to the fold.

5. In extensive reconstruction of the chin, the flap should extend to the vermillion border even if healthy intervening tissue must be sacrified.

6. With scar tissue extending to both sides of the face, the replacement should be symmetrical, even if healthy tissue must be removed.

7. To cover the entire chin, from ear to ear, with one piece of skin is difficult. The scar of division should be carefully planned in an esthetically inconspicuous place.

8. Suturing of the flap to the adjacent normal skin must be meticulous in order to leave fine scars.

9. The flap should be tacked down to the underlying skin with catgut sutures to avoid shifting and the formation of hematomas.

10. The flap can be thinned and modeled step by step after the transfer has been completed.

11. At the angles of the mouth, small portions of healthy skin should be spared for better function.

Both ordinary skin grafts and tubed grafts have various advantages and disadvantages. The use of one to the exclusion of the other is impossible.

JOHN WILTSIE EPTON, M.D.

Greeley, P. W.: Plastic Repair of Extensor Hand Contractures Following Healed Deep Second-Degree Burns. *Surgery*, 1944, 15: 173.

Deep second-degree burns of the dorsal aspects of the hands and fingers are quite frequent in modern warfare. While burns of this type heal spontaneously, a thick fibrotic covering commonly develops thereafter, which does not respond to conservative therapy. Replacement of the damaged skin by a single massive, thick split-thickness skin graft gives an excellent final result. J. M. MORA, M.D.

Pickett, W. J., and Meyers, M. P.: Further Experience with Pilonidal Cysts at Fort Sill, Oklahoma. *Am. J. Surg.*, 1943, 62: 387.

In the treatment of pilonidal cysts at an Army station hospital, several methods of closure after complete excision were employed, viz., open packing, primary closure, skin grafting of uninfected cases at the time of operation or as soon thereafter as possi-

ble, and partial primary closure by suture of the skin to the fascia. In the cases in which open packing was used the postoperative hospitalization averaged twenty-six days, with extremes of from seven to fifty-eight days. This is one way of securing complete cure when the time factor is not considered too important.

The authors were able to use primary closure in only a few uninfected cases. The postoperative period involved from two to three weeks of hospitalization, which is long, but it was considered necessary to make sure that the wounds were completely and thoroughly healed.

Two cases were treated with skin grafting but the difference in results did not seem worth while in view of the greatly increased amount of work involved.

As a compromise, partial primary closure, with suture of the skin edges to the deep fascia and periosteum, was tried. This generally results in a wound of about half the original size, and a vaseline pack is employed. Considerable sulfanilamide is used at the time of operation and during the dressings. This type of procedure yields a very comfortable postoperative period and the men are out of bed in a short time; however, the men at Fort Sill were hospitalized for a considerable period of time because it was desired that they be discharged with healed wounds.

The question of recurrences cannot be settled at this time. JOHN W. EPTON, M.D.

Kay, A. W.: Heat in the Treatment of Shock. *Brit. M. J.*, 1944, 1: 40.

This report is an investigation upon healthy adults exposed to heat under a "heat cradle" to determine the effects of this treatment, which is usually applied in the treatment of shock. Observations were made on the (1) arterial blood pressure, (2) venous blood pressure, (3) pulse rate, (4) oral temperature, and (5) patient's clinical condition.

Fifteen normal subjects were exposed for one hour to the heat cradle, during which time saline solution was administered intravenously to 10 and plasma intravenously to 5. A progressive rise in the pulse rate and venous pressure, together with a progressive fall in the arterial blood pressure, was noted in all cases. Nausea, vomiting, dehydration, headache, perspiration, muscular pains, and exhaustion were present in all cases and in some the symptoms were severe.

The author concludes that these findings contraindicate the use of heat in the treatment of patients suffering from traumatic shock.

BENJAMIN GOLDMAN, M.D.

Fox, C. L., Jr.: Oral Administration of Sodium Lactate in the Treatment of Burn Shock. *J. Am. M. Ass.*, 1944, 124: 207.

The shock syndrome which follows severe burns is accompanied by hemoconcentration and diminished plasma volume. Intravenous administration of plasma does not invariably correct the hemoconcentration which occurs.

The procedure used in this study is briefly as follows: morphine sulfate, ¼ gr. (0.016 gm.), was administered by hypodermic injection to patients on their admission for severe pain (less to children). Blood was taken at once for immediate and subsequent analyses. The patient was placed on and covered with a sterile sheet, but no blankets nor heat were applied. Large amounts of the chilled isotonic (one-sixth molar) 1.75 per cent sodium lactate solution were given by mouth at once and at fifteen-minute intervals thereafter on schedule. This solution was prepared by emptying a bottle previously filled with 72 gm. of sodium-lactate syrup into a 4-liter bottle, which was then filled with cold tap water. Sodium-lactate syrup varies in composition, frequently containing but 60 to 65 per cent of sodium lactate, in which case 110 gm. were used. Storage of large quantities of the isotonic solution, which may become sour, was thereby avoided. The burns were rapidly freed of any loose tissue, covered with a local application, and bandaged. Blood pressure and samples of blood were taken at frequent intervals during the first twenty-four hours. A careful record of fluid intake is imperative, and an exact schedule is used so that approximately 7 to 10 liters (from 10 to 15 per cent of the body weight) of the isotonic sodium lactate are administered within the first twenty-four hours. Any vomiting (which frequently occurs in severe burns) was treated by the administration of more fluid. Frequently a small Levine tube was passed through the nose and connected with a drip apparatus, so that the sodium lactate was administered constantly. The urinary output was carefully watched and all urine collected. Fluid administration in the subsequent days was adjusted to obtain 1 to 2 liters of urine daily. When food was tolerated, a high protein diet supplemented in extensively burned patients by from 50 to 100 gm. daily of amino acids was given.

The results were so successful as to warrant further extensive trials of this method of treatment. There was but 1 death among 17 cases of full-thickness burns. HAROLD C. OCHSNER, M.D.

Rhoads, J. E., Wolff, W. A., Saltonstall, H., and Lee, W. E.: Further Experiences with the Use of Adrenocortical Extract in Burn Shock. *Ann. Surg.*, 1943, 118: 982.

Further studies on the use of adrenocortical extract in conjunction with plasma in the treatment of burn shock have not fulfilled the promise of an earlier, smaller group of cases. Twelve patients with extensive superficial burns were given adrenocortical extract. At about the twelfth hour after the occurrence of the burn, the plasma deficit was calculated, and approximately this amount of plasma was administered between the twelfth and thirtieth hour. The plasma deficit was again calculated, and the increment in circulating plasma was compared to the amount transfused in order to estimate the amount

of plasma retained. Results were compared with those in a control group in which adrenocortical extract was not used. Local treatment consisted of tanning with one of the commonly used agents.

The mean per cent plasma retention for the treated series was 57 in terms of volume as compared with 57 per cent for the control series. In terms of grams of circulating plasma protein the mean per cent retention for the treated series was 46 as compared with 57 per cent for the control series. Early administration of adrenocortical extract showed no advantage.

This study is not concerned with the effects of adrenocortical extract on toxemia, but suggests that it is not indicated for routine use in the management of burn shock. JOHN L. LINDQUIST, M.D.

Seelig, M. G., Verda, D. J., and Kidd, F. H.: The Talcum-Powder Problem in Surgery and Its Solution. *J. Am. M. Ass.*, 1943, 123: 950.

In this report the authors re-emphasize the very serious surgical hazards incident to the use of talc as a dusting powder for rubber gloves, and recommend potassium bitartrate as a substitute powder.

From the surgical literature dealing with talc it is quite evident that this powder creates serious postoperative hazards, particularly intestinal obstruction. Most of the reports give detailed description of the surgical complications due to talc, with practically no stress on the possibility of substituting for it some satisfactory, innocuous powder. It has been estimated that a fingertip of a carelessly prepared glove often contains as much as 100 mgm. of talc. Studies by Weed and Groves show that (a) in 74.4 per cent of all operations, some gloves are torn, and (b) 22.6 per cent of all gloves used show rents or punctures. Talc may also come from the surface of gloves or possibly from gauze sponges or pads contaminated with talcum powder.

Granulomas resulting from talc implantations have been described elsewhere than in the peritoneal cavity. They have been found in the rectum, vagina, cervix, brain, and in healing wounds.

A brief historical summary is presented.

The authors believe that a substitute for talc must be based on two fundamental considerations:

1. The substitute powder must possess such a degree of actual or potential solubility as to be disposed of rapidly and completely by some form of peritoneal or tissue absorption. If this is not true, the powder collects in the peritoneal cavity as masses or plaques which induce foreign-body granulomas, which in turn result in adhesions; or the powder sets up foreign-body reactions in wounds or mucous membranes.

2. The powder must possess such a degree of insolubility as to withstand steam sterilization without losing its dusting property, which serves to prevent the adherence of glove surfaces.

Twenty-four different powders and 7 different starches were tried in this study. These studies were directed toward determining primarily whether or not the various powders possessed such dusting properties as to permit the gloves to come out of the autoclave in adequate condition. Many of the powders that were tried met this test successfully because most of them are sufficiently soluble. With the starches, however, gelatinization resulted from sterilization and rendered the gloves unusable.

The second step consisted in testing the physically satisfactory powders on white rats by injecting sterile water suspensions of varying concentrations into the peritoneal cavities. All of the powders that had successfully met the test of steam sterilization produced pathological lesions in the peritoneal cavities except potassium bitartrate. This powder was rapidly disposed of without its causing even the slightest toxic or physical effects, either local or general. Coarse mesh (210 to 270) potassium bitartrate (cream of tartar) is recommended. The authors have used bitartrate powder in operating rooms for some time and have found it satisfactory. It can be resterilized more than one-half dozen times without deterioration of the powder. In addition, potassium bitartrate is highly bacteriostatic. In experiments by the authors it was shown that this powder inhibits markedly the growth of the staphylococcus aureus and the escherichia coli. Talc has no antibacterial action.

There is some evidence that potassium bitartrate tends to shorten the life of the rubber glove. It was found by the authors that tartrated rubber gloves would stand from 7 to 10 sterilizations, whereas talcum powder permitted from 10 to 20 sterilizations.

DWIGHT E. CLARK, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

McDonnell, J. F., Wallace, D. A., and Andes, J. E.: Nail-Puncture Wounds. *J. Am. M. Ass.*, 1943, 123: 894.

In a nine-month period of much rain and mud, 721 men were treated for nail punctures with satisfactory results. The average disability was only 0.072 day per injury.

The treatment was as follows:

The area surrounding the puncture wound was scrubbed well with liniment of soft soap and water, and then wiped dry with sterile gauze. With pointed scissors and thumb forceps the edges of the wound were trimmed away through the entire thickness of the skin to leave a round hole, the edges of which did not approximate. The wound was then probed gently with a rough probe. This served to remove small particles of foreign matter and to determine the length and direction of the puncture. A blunt needle attached to a syringe was inserted in the direction and to the depth discovered by the probing. From 1 to 2 cc. of antiseptic solution (hydrogen peroxide was found satisfactory) were injected and allowed to return around the needle, to irrigate the wound from its deepest point outward. This served to wash out small foreign bodies and other contaminants. A dry sterile dressing was then applied, and

the patient told to return to work. Tetanus antitoxin (1,500 units) was given in 54.4 per cent of the cases. It was used when punctures were exceptionally deep or showed gross contamination or signs of infection. Men with severely contaminated wounds were given mixed gas-bacillus and tetanus antiserum.

Local infection developed in 43 patients; in 6 of these, the infection was severe enough to cause loss of time from work. No case of tetanus developed. There were no deaths. SAMUEL KAHN, M.D.

Kern, R. A., Norris, R. F., Montgomery, H., Wigton, R. S., Ferguson, L. K., and Brown, R. B.: The Treatment of Burns; A Discussion Based on Experience with 360 Cases Seen on Board a U. S. Hospital Ship. *Naval Med. Bull.*, 1944, 42: 59.

The data and opinions presented in this article are based on experience with 360 cases of burns incurred by naval and military personnel in battle or under conditions of active duty both afloat and ashore, and treated by various methods commonly in use. Burns constitute an important group of casualties in naval warfare. Therefore, preparedness for treating such cases in large numbers and at a moment's notice is a prime duty of all naval medical officers afloat and in advance medical facilities ashore.

Such preparedness must include both a store of supplies and an organized and trained personnel.

In order to distribute the working load best, the treatment of burn cases in hospital ships and in field, evacuation, mobile, and base hospitals in advanced areas should be assigned to the medical and not to the surgical service. This in no way detracts from the closest co-operation between the services in the management of these cases.

Since burn patients do not die of their burns, but of shock, toxemia, or sepsis, the first step is to prevent, or to recognize promptly and treat, these several complications.

Pressure dressings can prevent the development of edema to some degree as well as reduce an existing edema, and so lessen the occurrence and severity of shock. This is true particularly in patients with burns of the extremities over which an elastic bandage can easily be applied. The frequency with which the use of elastic pressure bandages is possible is shown by the fact that of 360 burn cases, 333 presented some involvement of an extremity.

Shock must be treated by adequate amounts of plasma, the dosage being based on frequent hemoglobin determinations.

The use of morphine in the relief of pain calls for an initial dose of not more than ½ gr., subsequent doses of not more than ¼ gr., and the meticulous recording of each dose given, on a tag attached to the patient.

Toxemia is most effectively prevented and met by an adequate, but not excessive, fluid intake (about 4 liters) and salt by mouth and, if needed, by vein, sufficient to replace the salt which is lost. In the absence of control by blood analysis, 5 to 10 gm. a day are called for.

A prime requisite in guarding against infection of burn areas and possible sepsis is the use of an aseptic technique in dressing burn cases, which includes the masking of the attendant personnel.

The preparation of the burn area for the definitive local treatment calls for simple cleansing, with mineral oil and sterile cotton waste to remove fuel oil, and plain soap and water, and a minimal débridement (cutting away blisters) to avoid further shock.

In the interest of simplicity of preparedness and application, and of economy of space and materials, the method of local treatment best suited to naval conditions is one that is applicable to all parts of the body, to patients with coexisting surgical lesions such as wounds and fractures, to uninfected burns (as primary treatment), and to burns that have become infected or that require preparation for and treatment after skin-grafting (as secondary treatment).

A number of the current methods of local treatment do not fulfil one or more of these conditions. The authors mention, particularly, tannic acid, paraffin-wax, and triple dye treatment. Tannic acid must not be used on the face, ears, or hands. Yet of 360 patients only 69 had burns that did not involve these parts. None of the three methods mentioned is applicable to an infected burn, to the preparation for or after-treatment of skin-grafting, or to a patient with wounds or fractures.

Sulfathiazole, either in 3 per cent ointment with a water-soluble base or as a dusting powder (preferably in the microcrystalline form), with wet saline dressings, meets all of these requirements when used in the manner set forth in this communication.

Skin-grafting should be done early to prevent scar formation.

Many burns could be prevented in naval actions by attention to: full clothing at battle stations; the use of antiflash gear that has been fireproofed; and by the constant availability of gloves, which are to be worn by those whose efficiency would not be reduced thereby and carried by the rest for possible use in case of fire or when sliding down ropes, since burns of the hands are responsible for the longest periods of disability. J. M. MORA, M.D.

Macfarlane, R. G.: Human Fibrin as Dressing for Burns. *Brit. M. J.*, 1943, 2: 541.

In an attempt to control the copious and continued oozing of fluid from a burned surface, human fibrin was selected as a "physiologically ideal" impervious dressing. The finished membrane is a tough, elastic, glistening white sheet when wet; when dry it becomes transparent and brittle. The author goes into careful technical detail concerning the preparation, sterilization, preservation, and application of the membrane. For controls, experimental burns were produced on 2 human patients.

The author concludes that the covering of burned areas with an adhesive membrane of human fibrin is a comparatively easy procedure. From the results, however, it will be seen that the clinical advantage

over orthodox treatment is so slight as to make the trouble involved in the preparation and application hardly worth while. The membranes relieve pain rapidly and form comfortable dressings, but the same can be said of many other applications. They may, to a certain extent, reduce fluid loss during the first twenty-four hours, but it would probably be more economical to transfuse the patient with the plasma required to make the membrane. In the cases that became infected the membranes were rapidly lysed. In favorable cases the membrane dried into a scab, and healing proceeded beneath this. Even so, however, healing did not appear to be much more rapid than was the case in other areas treated differently.

The problem of the fluid loss from burned areas still remains, and its causation is of obvious interest and importance. That it is due mainly to paralysis or disordered function of the capillaries seems probable. Attempts to restore this capillary function might be therapeutically profitable.

JOSEPH GASTER, M.D.

Posch, J. L., Stofer, B. E., and Hirshfeld, J. W.: Salmonella Cholerae Suis as a Cause of Indolent Subcutaneous Abscess. *J. Am. M. Ass.*, 1943, 123: 813.

Salmonella cholerae suis, which is more commonly known as salmonella suipestifer and is normally found associated with a virus in the hog's intestinal tract, was described by Salmon and Smith in 1885. The most common type of sporadic infection is a bacteriemia which simulates typhoid. Numerous other manifestations have been reported. Among them are pneumonia, pyarthrosis, osteomyelitis, endocarditis, meningitis, cholecystitis, splenic abscess, and infection of the urinary tract. Salpingitis, subdural abscess, infection of myoma of the uterus, and acute appendicitis have also been described. Exceedingly rare are reports of salmonella infection involving the skin and subcutaneous tissues either following septicemia or occurring without antecedent infection of the blood stream.

The authors report a case of indolent subcutaneous abscess due to this organism. The case is interesting as the patient was seventy-three years old and the majority of previously reported localized infections have been in children. A retired negro laborer complained of a swollen and painful left wrist. He stated that forty years previously, while he was working in a stone quarry, a piece of rock hit him on the back of the left wrist and severed a tendon. A foreign body was deeply embedded in the wound; the wound healed uneventfully, but a small nodule appeared in the scar. This nodule had swollen intermittently for forty years, but application of liniment had usually caused the swelling to recede. About a month before the patient came to the hospital, a heavy cooking pot fell on his wrist and injured the old scar. The next day the area was painful and swollen, and the swelling subsequently increased. The left wrist at the radial aspect showed a prominence about 2 cm. above the surface of the arm which was between 2 and 3 cm. in diameter. It was indolent and soft, moderately painful, and fluid to palpation. The entire forearm was somewhat swollen. The patient was seriously ill and had a spiking type of temperature. X-ray examination revealed a foreign body in the left wrist. Continuous hot soaks were applied to the arm, and the patient was given sulfathiazole. His temperature returned to normal the day before dismissal. After the patient's discharge from the hospital the arm continued to be swollen, painful, and tender, and did not improve on supportive measures.

One month later the examination revealed a large, apparently fluctuant mass occupying the entire dorsum of the left wrist. The mass was tender, and motion at the wrist was slightly limited.

Under local anesthesia a longitudinal incision about 4 cm. long was made through the skin and subcutaneous tissue. Several cubic centimeters of thick greenish purulent material were encountered in the center of the mass. The mass itself consisted of gray-green rubbery tissue which appeared grossly to be tuberculous. A portion of this was removed for microscopic examination, and a pathological report of pyogenic granuloma and organized hematoma was returned. The organism was identified as salmonella cholerae suis, variety of Kunzendorf. A few months later the draining sinuses were still present at the site of the original lesion on the dorsal aspect of the wrist.

JOSEPH K. NARAT, M.D.

Hollenbeck, W. F., and Turnoff, D.: Actinomycosis Treated with Sulfadiazine. *J. Am. M. Ass.*, 1943, 123: 1115.

Any agent that influences the course of actinomycosis favorably is worthy of note. The results achieved by sulfadiazine in the case reported—a case of actinomycosis of the cervicofacial type—seem remarkable. The diagnosis of the disease was established by the laboratory finding of the ray fungus on direct smear and culture.

The patient was given sulfadiazine by mouth in 1-gm. doses, every four hours. A week later, the quantity was cut to 1-gm. doses given four times daily. This dosage was maintained for the duration of the treatment. In all, the patient received 500 gm. of sulfadiazine, administered over one hundred and twenty consecutive days. It was fully two weeks before any noticeable change in the lesions could be observed. Later, however, the abscesses disappeared and the scars actually dissolved, the skin becoming practically normal.

Whether the abdominal cases of actinomycosis, which have a much greater mortality, and the thoracic cases, which have by far the poorest prognosis, will also respond favorably to sulfadiazine is still to be determined.

It should be noted, incidentally, that a moderate dose of sulfadiazine, administered daily for four months, had no untoward effect on the kidneys, the blood, or the health in general

SAMUEL KAHN, M.D.

Fig. 1. Appearance six days after onset. Note denudation. Skin is covered with zinc oxide.

Kasselberg, L. A.: A Severe Pemphiguslike Reaction following the Administration of Sulfamerazine. *J. Am. M. Ass.*, 1943, 123: 1035.

A near fatal pemphiguslike reaction to sulfamerazine after the administration of only 4 gm. over a period of forty-eight hours is reported.

A twenty-year-old white male was first treated for acute gonorrhea on August 30, 1943 by means of calcium gluconate given intravenously and sulfathiazole (8 gm.) daily for one week. Because the penile discharge was unchecked he was placed on a mild silver proteinate injection and all sulfonamides were stopped. On September 27 he was started on sulfamerazine (2 0.5 gm. tablets every twelve hours). After only 8 tablets had been given, in forty-eight hours, a generalized macular rash, not unlike that of measles, was noted; all mucous membranes were fiery red and there were some tiny blebs in the mouth; the temperature was 102° F. The conjunctiva of both eyes was edematous and injected. In about thirty-six hours there were many bullae over the body which were filled with a clear straw-colored fluid. The temperature was of a septic type, varying from 105° to 97°F. By October 7 the condition began to improve and the temperature leveled off by lysis. The patient was discharged on October 23 greatly benefited. He still had a purulent penile discharge, but no gonococci in smears. The only sequelae were conjunctival adhesions to the left eyeball.

In 1942 the patient had had purulent otitis media, which had been treated successfully with sulfathiazole without reactions.

The blood sulfamerazine on October 2 was 2.4 mgm. per 100 cc.

Treatment consisted in the intravenous administration of fluids, sedation, and the administration of multiple vitamin and iron capsules by mouth, zinc oxide to the skin, boric-acid packs to the eyes, and phenacine hydrochloride and ephedrine ointment to the eyes. Parenterally, liver extract, massive doses of vitamin B complex, ascorbic acid, menadione, and vitamin D were administered.

The authors thought that since there had been no toxic symptoms after sulfathiazole medication, the rapid and acute onset of the reaction after only 4 gm. of sulfamerazine had been given over a period of forty-eight hours probably indicated some type of allergic manifestation. DWIGHT E. CLARK, M.D.

Dawson, M. H., Hobby, G. L., Meyer, K., and Chaffee, E.: Penicillin as a Chemotherapeutic Agent. *Ann. Int. M.*, 1943, 19: 707.

In 1941 the Oxford workers on penicillin described a method for the small scale production of material suitable for therapeutic use in man. Their experiments showed that penicillin was active in remarkably high dilutions, that it possessed little toxicity, and that its action was not inhibited by blood, pus, or tissue derivatives.

The work of the authors was started in 1940 and is a confirmation in part and an extension of the work of the English investigators.

After a careful description of the method of preparation of "penicillium notatum," the article explains that experiments have shown that penicillin is highly effective against Gram-positive organisms, both aerobic and anaerobic, and against gonococci and meningococci. The action of penicillin appears to be either bactericidal or bacteriostatic, and depends on the conditions of the experiment. It is active in extraordinarily high dilutions. Experiments with highly purified preparations of penicillin have shown that amounts as little as 0.03 μg. per cc. are sufficient to inhibit the growth of a 10^{-2} dilution of a culture of hemolytic streptococci containing from 200 to 300 million organisms per cubic centimeter. It is many thousand times as effective as any of the sulfonamides, its activity being comparable to that of gramacidin and tyrocidin.

Experiments have shown that penicillin causes an actual diminution in the number of organisms, whereas sulfanilamide and sulfathiazole cause only a decrease in the rate of multiplication of the organisms. Further experiments indicate that the action of penicillin is not inhibited by blood or serum.

In experiments with mice it was shown that penicillin is effective against hemolytic streptococcal infections when given intraperitoneally as well as when given subcutaneously.

Treatment of infected mice was successful not only when the drug was given simultaneously with or

shortly following infection, but also when administered as late as eight hours after infection.

Work with the anaerobic spore organisms shows that whereas small amounts of penicillin protect against large numbers of highly virulent hemolytic streptococci, comparable amounts will give partial or complete protection against only two or three lethal doses of the clostridium welchii and clostridium septique.

The toxicity of penicillin has been tested in mice, guinea pigs, rabbits, dogs, and man. No toxicity was observed with amounts far beyond the range of therapeutic dosage.

The rapidity of excretion of penicillin through the kidneys is a serious obstacle in its therapeutic use. When this drug is administered by intravenous or intramuscular routes it is rapidly lost from the blood stream, none being detectable after from two to four hours. Efforts are being directed toward the preparation of compounds which will slowly release active penicillin into the circulation.

Clinical use of penicillin has been greatly hampered by two facts: (1) the small yield, and (2) the desire to provide as much material as possible for chemical work. Penicillin has been proved to be effective in man when given intramuscularly, intravenously, and intrathecally. It has also proved effective when administered directly into joints and serous cavities as well as in local applications. It is of value in the treatment of infections due to hemolytic streptococci, pneumococci, gonococci, meningococci, and staphylococci. In particular, it has proved effective in cases resistant to sulfonamide therapy. The number of cases so far treated is small, but the results are highly encouraging. Up to the present time no serious toxic effects have been observed. JOSEPH GASTER, M.D.

Lyons, C.: Penicillin Therapy of Surgical Infections in the U. S. Army. *J. Am. M. Ass.*, 1943, 123: 1007.

This report is a summary of the experiences of trained observers of penicillin therapy from several general hospitals within the Zone of the Interior. Special facilities were made available in the wards and laboratories, and surgical dressings were carried out under operating-room conditions.

PENICILLIN

Methods of administration. Penicillin was given intravenously, intramuscularly, intrathecally, and locally.

No contraindication to the intramuscular route was observed.

The constant intravenous method of treatment was preferred for immediately life-endangering infections. Penicillin was dissolved in 5 per cent dextrose or isotonic solution of sodium chloride for constant drip administration, or injections of concentrated solutions were made at frequent intervals, directly into the tubing or into an adapter valve in the tubing.

For local use the usual preparation contained 250 units per cubic centimeter. The single daily application was usually adequate to keep the wound clean and free from pyogenic cocci. Penicillin was injected through tubes, incorporated into ointments, and applied as a wet dressing. Both calcium and sodium salts were used.

The intrathecal route was recommended for patients with meningitis.

In the early experiences there were untoward reactions attributable to toxic impurities. The untoward complications ascribable to penicillin were uncommon and included the following:

1. *Urticaria.* The most common single complication was urticaria and it occurred in 12, or 5.7 per cent, of 209 cases. It occurred during every week of treatment, continued for from three to five days, and was independent of continuance or cessation of treatment. Subsequent courses of penicillin therapy in patients with a history of urticaria during the first treatment were not associated with recurrent urticaria. The complications associated with urticaria were fever and abdominal cramps. The fever was present only when the urticaria was severe and did not usually exceed 101°F.

2. *Fever without urticaria.* In a few patients fever without urticaria was noted during the first five days of treatment.

3. *Transient azotemia.* This was of no clinical significance.

4. *Thrombophlebitis.* At the site of constant intravenous injection thrombophlebitis occurred frequently. The complication may be avoided by the use of dilute solutions of penicillin and a daily change of the position of the needle. The hazard of pulmonary infarction as a consequence of thrombophlebitis in the lower extremity has led to the recommendation that all intravenous injections be given in arm veins.

The greatest difficulty attends precise definition of therapeutically effective dosage for penicillin. The following suggestions in regard to dosage were recommended:

1. *Streptococcic infections.* The groups of resistant and susceptible species of streptococci were outlined. Adequate therapy for susceptible infections was provided by 90,000 units of penicillin daily, given intramuscularly at the rate of 15,000 units every four hours.

2. *Staphylococcic infections.* As a group the staphylococci required two to four times as much penicillin for inhibition as did the susceptible strains of streptococci or pneumococci, but some strains of staphylococci were extremely sensitive. The hazard of penicillin fastness dictated intensive and effective initial dosage for all infections, particularly staphylococcic infections. For bacteriemic infections the constant intravenous treatment recommended was an initial dose of 25,000 units and from 5,000 to 7,500 units every half hour thereafter up to a total of from 240,000 to 360,000 units daily. As much as 600,000 units daily was required for such infections. As

progress warranted or as an alternative method for maintenance, a dosage of 25,000 units every three hours provided 200,000 units daily. The latter dosage was routine for all nonbacteriemic staphylococcic infections treated with the penicillin of present potency.

3. Clostridial infections. Systemic penicillin therapy in dosages of 200,000 units daily controlled anaerobic cellulitis but did not arrest suppuration as dramatically as in the cases of pyogenic coccic infection. Local therapy was a necessary supplement to systemic therapy; local therapy alone was not as effective as combined therapy. Control of the anaerobic infection usually followed wound revision and sequestrectomy. The subsidence of inflammation was entirely clinical, for the clostridia persisted in the wound throughout the period of healing in spite of intensive local therapy.

PENICILLIN THERAPY OF ACUTE INFECTIONS

The results in the treatment of acute infections were as follows:

Bacteriemia. Six of 9 patients with staphylococcemia recovered. The 3 deaths included 2 instances of endocarditis.

Of 4 patients with hemolytic streptococcus bacteriemia, 3 recovered. These cases had failed to respond to sulfadiazine.

Of the remaining 6 patients with bacteriemia due to a variety of organisms, 3 recovered.

Staphylococcic infections without bacteriemia. Sixty-nine, or 87 per cent, of 79 patients showed a favorable response to penicillin therapy. One patient with third-degree burns died.

The largest groups of infections were as follows:

Of 21 cases of wound infection, 17 improved; of 12 abscesses, 11 improved; of 12 infections of the skin and subcutaneous tissues, 11 improved.

Eleven of 12 patients with osteomyelitis were benefited as judged by sterilization of the pus, and complete or partial healing of the sinuses.

At the present time it seems likely that the penicillin therapy of chronic staphylococcal osteomyelitis of the long bones may require surgical intervention with incomplete or primary closure of the wound. There is reason to believe that penicillin may effect subsidence of osteomyelitis of the flat bones without surgical intervention in the absence of sequestra.

Hemolytic streptococcal infections without bacteriemia. Satisfactory bacteriological sterilization was achieved in the 11 cases. One patient with empyema died.

Mixed staphylococcal and hemolytic streptococcal infections. Six of 8 cases responded favorably and 1 wound infection was not influenced. One patient with burns died.

Anaerobic cellulitis. Two patients with low-grade infections of the subcutaneous tissues due to the clostridium perfringens responded favorably.

Lung abscess. There was no effect on 2 patients with putrid lung abscess; 2 pyogenic streptococcal lung abscesses healed.

Intraperitoneal infections. Two of 6 cases improved.

Infections of unknown etiology. Of 19 patients, 12 were benefited.

Miscellaneous infections. Malaria due to plasmodium vivax was not affected. Four patients with actinomycosis were benefited by treatment. Chronic ulcerative colitis failed to respond in 2 instances.

THERAPY OF CHRONIC INFECTION IN GUNSHOT FRACTURES

Patients with septic gunshot fractures were studied with particular care.

Nutritional depletion. The weight loss was considerable, varying from 5 to 30 kgm. and gain in weight was rarely apparent before the sixth week of convalescence.

On admission the interstitial fluid volume was too great, and during convalescence it slowly decreased. The sedimentation rate was correlated more closely with improvement than any other laboratory determination.

The blood volume was always small but fluctuated considerably in size.

There was a deficit in the total quantity of circulating hemoglobin, but a normal or nearly normal quantity of plasma protein was present. The major deficiency was hemoglobin.

The urinary nitrogen was high (from 15 to 20 gm. daily). A positive nitrogen balance was attained by any method that provided an intake of 130 gm. of protein or more per day. One of the important consequences of penicillin therapy was the improved appetite. Penicillin therapy did not alter the nitrogen balance per se but did favor a positive balance in consequence of an improved appetite with controlled infection.

Effective restoration of hemoglobin did not result from a positive nitrogen balance unless the penicillin was given to control infection. Frequent transfusions of from 500 to 1,000 cc. of whole blood were necessary during the preoperative and postoperative periods. A judicious combination of whole blood and plasma given in 1,000 cc. quantities on the day before operation, the day of operation, and the day after operation was necessary to maintain the blood volume and a positive nitrogen balance. Similar quantities of whole blood were necessary once or twice a week until the hemoglobin values were restored and maintained at a normal level.

Bacteriological characteristics of the infection. The bacteria present in the wounds were variously susceptible to penicillin and were important limiting factors in the choice of operative procedures. The staphylococci and hemolytic streptococci were controlled effectively in the great majority of instances. The Ps. pyocyanea was not inhibited, but rarely did more than delay wound healing. The proteus and the faecalis groups of streptococci were insensitive to penicillin.

The paramount problem in the penicillin therapy of septic gunshot fractures was putrid wound infec-

tion. It was impossible to remove completely the organisms producing this condition in wounds. A combination of local and systemic penicillin therapy produced clinical improvement but suppuration continued until sequestrectomy was performed. Attempts at wound closure invited anaerobic cellulitis. Local therapy was continued until the wound was healed to prevent secondary infection. Meticulous care of the wounds was necessary.

ERNEST E. ARNHEIM. M.D.

Shumacker, H. B., Jr., and Bethea, W. R., Jr.: Some Studies with Zephiran; With Particular Reference to Its Use in Time of War. *Surgery*, 1943, 14: 931.

Zephiran is a mixture of high molecular alkyldimethyl-benzyl ammonium chlorides in which the alkyl group represents a series of homologous radicals derived from the fatty acids of cocoanut oil.

Zephiran is an amber-colored solid of soaplike consistency, marketed as a 1:10 concentrate, and readily soluble in water, alcohol, and acetone. The solution is colorless and almost odorless. It has a definite detergent, keratolytic and emollient action, and is not irritating to the skin. It is procurable and inexpensive. Soap exerts some inactivating influence upon zephiran, but zephiran is compatible with local anesthetic agents, the sulfonamides, and other substances with which it may come in contact in operative surgery. It is stable and active over a wide range of temperatures.

Since Domagk described the remarkable bactericidal property of this agent, a number of studies have confirmed its value as a germicide.

Zephiran for preparation of the hands of members of the operating team. The gloved hands of members of the operating team, prepared in various ways, were cultured. There were fewer hands from which positive cultures were obtained after brief scrubbing with 1:2,500 zephiran and a short soak in this solution, and after simply soaking the uncleansed hands in 1:1,000 zephiran for three minutes than there were after the most rigorous scrubbing with liquid green soap for eight minutes followed by soaking in 70 per cent alcohol for three minutes. Twenty-one per cent of the hands prepared by the usual soap-and-water and alcohol technique showed some growth of organisms. Of 71 hands prepared with 1:2,500 aqueous zephiran, 24 per cent showed growth of some organisms. Of 71 hands prepared with 1:1,1000 zephiran, only 7 per cent showed growth of organisms, only one colony growing out in each instance. It would appear that a brief soak in 1:1,000 zephiran brings about as good a preparation of the hands as the most rigorous soap and water scrubbing followed by soaking in alcohol, particularly if the soak in zephiran is preceded by a brief scrubbing in this solution.

After soaking in zephiran the hand has a very comfortable satiny feel which persists for several hours. Zephiran cleans the hands very well. It is more effective in removing oil and greasy debris than is soap and water. Used day after day over a long period of time it never causes any skin irritation and does not make the nails brittle or discolored.

Preparation of the skin of the hands and forearms of members of the operating team can be reliably carried out as follows:

Clean the nails, scrub the hands and forearms vigorously in aqueous zephiran (1:1,000) for three minutes, and soak them for three minutes in a basin containing this solution. Between clean cases, soak the hands in zephiran for three minutes. Scrubbing with 1:1,000 aqueous zephiran causes no real lather but a lather is obtained when one scrubs with 1:500 zephiran and this dilution may be employed for scrubbing if it is desired. If the hands are moistened with zephiran they can be easily slipped into powdered, dry sterilized gloves. It would seem likely that the film of zephiran on the hands would tend to inhibit growth of those organisms which remain on the skin.

Zephiran in the preparation of the operative field. The data given indicate that zephiran is a perfectly adequate agent for skin preparation. Furthermore, in-vitro studies demonstrate that it has greater germicidal efficacy than most of the antiseptics commonly employed for this purpose. In addition, its cheapness commends it. It has other very distinct advantages for the preparation of the skin. It is easily applied and cleanses the skin well since it has a certain detergent and keratolytic action. It has not been necessary to use any other cleansing agent with it. In numerous instances when patients have been brought in after traumatic lacerations received on the streets, areas covered with grease and dirt have been cleansed without difficulty. The solution is nonirritating to the skin. The authors know of no instance in which dermatitis, burn, or skin irritation has occurred because of the use of aqueous zephiran. In the dilute solutions which are employed it causes no reaction if it is allowed to run into the various body orifices and cavities. It has a great advantage in the preparation of the face, where it can be allowed to run into the external auditory canal, eyes, nose, and mouth without fear of tissue damage. One has no concern about the various body creases and folds as one does with so many of the antiseptics employed for skin preparation. One particular advantage of dilute aqueous zephiran is that it can be used freely in open wounds with apparently no deleterious tissue reaction.

Although the authors have found a 1:2,500 aqueous zephiran to be satisfactory for the preparation of skin, they are now using a 1:1,000 solution because in-vitro studies demonstrate that the 1:1,000 solution kills organisms much more quickly than does the 1:2,500.

Other uses of zephiran. A dilute aqueous zephiran (1:1,000 or 1:2,500) has a number of other uses. It is ideal for washing instruments and the hands of the operating team during the course of an operation. Whereas 76 per cent of basins of sterile water so used were found to be contaminated at the close of the operation, basins of 1:5,000 aqueous zephiran were

always sterile (Poppe). Similarly, aqueous zephiran is useful for wash basins necessary in the maintenance of isolation technique for cases of infectious disease. It is perfectly satisfactory for cleansing skin before venipunctures and various parenteral injections. Where instruments on dressing carriages are kept in some irritating sterilizing fluid, it is useful to keep alongside a jar of aqueous zephiran in which the instruments can be rinsed before being used. It is useful in compresses and soaks for various pyogenic skin lesions, and for epidermophytosis, particularly when it is associated with secondary infection. It is occasionally useful as a compress in clearing up infections of granulating areas. It works well as an irrigating solution for empyema and other abscess cavities. As a 1:20,000 solution it is satisfactory for urethral instillations. More concentrated solutions cause irritation. Instillations and tampons of 1:2,500 zephiran have proved useful in treating various pyogenic and fungus infections of the external auditory canal. Zephiran in concentration of 1:50,000 has been found ideal for the preservation of biological fluids such as bacteriophage and vaccines. If aqueous zephiran is used for the cold sterilization of instruments it is necessary to add some substance to prevent rusting. Some formalin solutions are so eminently satisfactory for cold sterilization of instruments that solutions of this sort should preferably be used for this purpose.

The use of zephiran in time of war. In time of war certain considerations assume a significance which is not existent in time of peace, such as the conservation of materials which are vital in the making of munitions and military supplies. Such a material is alcohol, of which enormous quantities are ordinarily employed in the practice of medicine. By more extensive use of substances such as zephiran, great quantities of alcohol can be conserved for purposes which are immediately more vital than these medical uses. Aqueous zephiran is a better germicidal agent and is more stable. Although 70 per cent ethyl alcohol by weight is a good germicide, it is difficult to maintain this exact concentration, and even slight changes in concentration render the solution totally ineffective against organisms.

Other considerations arise. Transportation of medical supplies assumes gigantic proportions. If 1:2,500 zephiran is employed, 250 gallons are available for use from each gallon of the concentrate transported to the medical unit. If 1:1,000 zephiran is used 100 gallons are available for use from each gallon transported. Another feature which is desirable in the various medical installations is a simplification of the pharmaceutical armamentarium. Zephiran can be utilized so effectively in place of alcohol and other germicidal agents which are ordinarily supplied, that it would seem worth while to substitute it for others. These considerations are particularly applicable in the forward medical installations such as the portable hospitals and clearing companies of the medical battalions. A further consideration is that of expense. In the base from which this article was written, zephiran, which is made in the United States and transported thousands of miles as 1:10 concentrate, can be purchased at such a price that 1:1,000 aqueous zephiran costs only approximately 13 cents per gallon and 1:2,500 zephiran about 5 cents per gallon. In contrast, the ingredients which are used in the preparation of liquid green soap bring the cost of this substance to about 25 cents a gallon, and the cost of alcohol is approximately 32 cents a gallon. Many of the germicidal agents employed are a great deal more expensive. Another consideration which is of special importance is that of preparation of the hands of the operating teams which can be carried out adequately with aqueous zephiran in any forward medical installation. ERNEST E. ARNHEIM, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Oechsli, W. R., and Kupka, E.: Roentgenographic Aspects of Monaldi's Cavity Aspiration in Pulmonary Tuberculosis. *Am. J. Roentg.*, 1943, 50: 733.

Monaldi in 1938 described a method of direct surgical approach to tuberculous cavities. This method includes the introduction of a special rubber cannula through the chest wall into the cavity; the catheter is anchored, and prolonged negative pressure is applied through the catheter.

A preliminary series of cases was first reported by the authors in 1940. Several hundred were thoroughly studied roentgenologically and with the aid of laminograms. The authors selected 17 of the cases in the original studies for presentation in this particular series.

Most of the cavities were located in the upper posterior lobes. Sometimes these cavities were so large that their location was obscured until a diminution in their size was produced. Cavities were of the balloon or tennis-ball type, and ranged from 5.5 to 15 cm. in diameter. Their walls were circular or oval, and presented the appearance of being under tension. This was indirect evidence that the bronchus was draining into the cavity. The walls were of uniform thickness and appeared to be composed of compressed alveoli.

An indication for the Monaldi aspiration from a roentgenological viewpoint is a balloon cavity located in the upper lobe; it should be accessible to an anterior approach and it should be surrounded by aerated lung. The disease should be of recent origin and no other cavities should be present. A contraindication to cavity aspiration is an associated atelectasis, or a very rapidly expanding cavity.

The cavity is localized by means of fluoroscopy, routine anteroposterior and lateral roentgenograms, and body-section roentgenograms. Under fluoroscopic control, the cavity is localized, and under aseptic conditions a trocar is inserted into the cavity. Films taken several days after aspiration sometimes reveal dramatic reduction in the size of the cavity. When a cavity is diminishing in size, there may be an increase in pleural thickening around it, which persists for months before it resolves. The increased density is most pronounced on the lateral and superior aspects of the cavity. The pleural thickening may be wedge-shaped with the apex directed toward the cavity. Such a density is referred to as "pleural spike."

Some cavities become so small that they are missed on the routine roentgenograms and are only to be demonstrated by laminograms. Body-section roentgenography also is of value in visualizing the presence and size of a sinus tract.

MAURICE D. SACHS, M.D.

Borman, C. N.: Ulcer in the Descending Duodenum. *Am. J. Roentg.*, 1943, 50: 752.

The small number of reported cases of ulcer in the descending duodenum diagnosed by roentgen examination compared to the incidence shown by autopsy suggests that in many instances these ulcers have been overlooked. Statistics are cited from various sources showing the incidence in autopsy studies and surgical experiences, and attention is called to the relative paucity of reports about extrabulbar ulcers in the extensive literature on duodenal ulcers.

It appears that the most frequent location of ulcers beyond the cap, based on both surgical and roentgen reports, is the region of the junction of the first and second portions of the duodenum on the inner border adjacent to the pancreas. Duodenal induration and spasm together with penetration and fixation of the ulcer bed to the pancreas with production of a relatively large inflammatory mass are prominent pathological features. In the more distal descending duodenum, ulcers have been demonstrated much less frequently, and while the location may be as low as the ampulla of Vater, the roentgen diagnosis of lesions at this level is exceedingly rare.

The infrequency of roentgen diagnosis of ulcers beyond the first portion of the duodenum as compared to their actual incidence may be related in part to the failure of the roentgenologist to conduct a thorough survey of this somewhat inaccessible region as well as to his failure to consider the possibility of the occurrence of ulceration at this particular level of the bowel. In certain instances ulcers of the descending duodenum may have been considered simple diverticula. Especially is this true in the concavity of the duodenum, since diverticula commonly occur in this particular area. Ulcer craters located in the medial wall of the upper descending duodenum may also have been interpreted either as barium retained in the lateral recess of a deformed duodenal cap or possibly as an ulcer crater in the cap itself.

The author reports 7 cases in detail with roentgenograms and comments on each case. In the cases reported the lesions were located on the upper and inner margins of the descending portion of the duodenum. Detection of the niche was the important factor in establishing the diagnosis of active ulceration. Secondary spasm, mucosal distortion, and medial retraction of the adjacent upper descending duodenum were present in every case.

The differential diagnosis from diverticula, cancer, visualized ampulla of Vater, and duodenitis is discussed. Consideration is also given to clinical characteristics of ulcers involving the descending duodenum, and attention is called to the fact that gross hemorrhage, often severe, is frequently associated with them. Macroscopic hemorrhage was a prominent feature in 6 of the 7 cases; in 3 instances

the degree of blood loss was unusually severe. Nocturnal pain was prominent in 4 of the 7 cases.

A. HARTUNG, M.D.

Schatzki, R.: Small-Intestinal Enema. *Am. J. Roentg.*, 1943, 50: 743.

The usual roentgenological methods do not permit visualization of the actual filling of the small intestines and observation of its partly or completely filled parts as is the case with other parts of the gastrointestinal tract. Therefore, opaque media have been introduced directly through a duodenal tube analogous to opaque-enema examination of the colon. Various authors have described such a procedure, and Schatzki has used it (at first without knowledge of the preceding publications) in approximately 75 cases. The results have been encouraging enough to recommend it as a routine procedure.

A Rhefuss tube with a metal olive tip is ordinarily introduced through the mouth and from 500 to 1,000 cc. of a 1 to 20 barium suspension are allowed to flow continuously through it during the period of fluoroscopic observation. In 35 normal cases the average time for the barium to reach the cecum was fifteen minutes; in 4 normal cases only did the filling require more than twenty minutes. In most pathological cases more time was required, the average time being thirty-seven minutes in 19 checked cases. Adequate precautions are urged to keep the total time of roentgenoscopy within the zone of safety.

The many advantages which this method of examination offers are described in detail. Some of the difficulties connected with it are also mentioned and contraindications to its use are discussed. Occasional reflux of the barium into the stomach may interfere with satisfactory conduct of the examinations.

Numerous roentgenograms of normal and pathological cases are included in the article, with comprehensive legends which serve well to illustrate some of the author's claims.

As a result of his experience the author concludes that the small-intestinal enema represents an improvement in the examination of the small intestine. If successful, it is better than any other available method for the study of morphological changes in the small intestine.

A. HARTUNG, M.D.

Klein, I.: Roentgen Study of Lymphogranuloma Venereum. *Am. J. Roentg.*, 1944, 51: 70.

In the female, lymphogranuloma venereum is carried not to the inguinal glands, but most frequently to the wall of the rectum. In the male, involvement of the rectum and sigmoid also is noted in the advanced stage of the disease. When this complication occurs, the outstanding clinical symptoms are tenesmus, constipation, and mucous and bloody stools. On examination one finds destruction of the mucosa, stricture above the anal orifice, distention of the rectal pouch, single and multiple perirectal and perisigmoid sinus formations, and fistulous tracts.

The author has performed systematic roentgen investigations in 24 cases of lymphogranuloma venereum accompanied by such complications, and he found the roentgen appearance to be quite clear and of distinct diagnostic value. The 24 cases are tabularly arranged to indicate the age, sex, race, history, the findings of physical examination, laboratory findings (Wassermann and Frei tests), pathological findings, and the roentgen findings. In some of the cases the Frei test proved negative; in other cases operation was performed because of a mistaken diagnosis, but all of the cases showed an advanced stage of the disease when the patients were examined by means of a barium enema. Five cases which showed the most typical findings are reported individually in brief résumés, and their roentgenograms are reproduced.

In connection with these cases, the author stresses the points of differential diagnosis from cancer and from ruptured multiple diverticula associated with cancer. Obviously the most important point is the duration of the disease. Lymphogranuloma venereum runs a chronic course and a history of from ten to twenty years is not infrequent, whereas a patient with cancer of the rectum will give, on the average, a history of from two to three years. The next point is that of location and extent of the involvement. About 75 per cent of the cases of cancer of the rectum have a circumscribed lesion on the anterior wall of the rectum, whereas lymphogranuloma venereum is more likely to start immediately above the anal orifice and to circle the entire circumference of the rectum; frequently the lesion extends into the sigmoid. In a few instances, a differentiation from stenosing scirrhous carcinoma which tends to infiltrate and circle the rectal wall will prove most difficult.

In conclusion, the author expresses the opinion that roentgen examination seems advantageous as an aid in establishing the diagnosis and extent of the disease and therefore it should be used routinely.

T. LEUCUTIA, M.D.

Tice, G. M., and Curran, E. J.: Treatment of Retinoblastoma; Radiation Therapy Supplementing Surgical Treatment. *Radiology*, 1944, 42: 20.

After brief consideration of the nature, incidence, and other facts relative to retinoblastoma, the authors discuss treatment with special reference to radiation therapy. Inasmuch as the tendency of these tumors to metastasize is not great, thorough local eradication may effect a cure. However, in many cases extension of the disease has progressed beyond the operative field, which would seem to be a good reason for routine postoperative irradiation. Although this tumor is not classified as radiosensitive, it has a degree of sensitivity, and inoperable cases ought to be irradiated as favorable results can be achieved even if they be only palliative. Whether radiation can add to the life expectancy remains to be seen. From their short period of observation the authors believe that it will.

Retinoblastoma involves both eyes in a considerable number of cases. When this occurs the alterna-

Fig. 1. Recurrent retinal glioma protruding from the left orbit.

Fig. 2. Regression of retinal glioma following x-ray therapy.

tive of recommending removal of both eyes as a life-saving procedure, or of attempting to destroy the tumor and at the same time conserving vision in one eye, presents itself. The latter involves removal of one eye and irradiation of the other. Reports of cases in which this was done are cited.

The literature relative to the treatment of retinoblastoma by radiation is reviewed at some length. The authors' method of irradiation was used (1) to prevent recurrence following enucleation of an eye because of retinoblastoma and (2) to preserve vision in the remaining, least involved eye when the tumor was bilateral; it is described in detail. A summary of data on 20 cases seen in the University of Kansas Hospitals is tabulated and case histories are included.

The authors summarize their experience as follows:

Of 20 cases, half of which were bilateral, 15 received radiation therapy supplementary to surgery. Seven of the 15 patients are living. One treated by enucleation alone is living. Three of those who had evidence of tumor in each eye are living with vision in the remaining eye, the other eye having been enucleated. One of these, who was treated with x-rays and who has been followed up for a period of more than two and one-half years, has 20–50 vision in the remaining eye. One patient was treated with radium needles imbedded about the periphery of the remaining eye. He has been followed up for seven years. A cataract has developed which is being treated. At present he can distinguish trees and other large objects. This child, incidentally, had extensive infiltration into the optic nerve of the enucleated eye. The third patient, who received one x-ray treatment and later was treated with small radium packs, is alive sixteen and one-half years following treatment, with 3–60 vision. One child treated with x-rays showed almost complete regression of the tumor in the remaining eye. Unfortunately he died of bronchopneumonia after having been followed up for more than two years. One patient who had a recurrence in the stump of the nerve five months after enucleation now presents a nine-year cure. He was treated with interstitial irradiation of the optic nerve head.

CONCLUSION

Radiation therapy of retinoblastoma as a supplement to surgical removal is advocated. Routine implantation of radium adjacent to the optic nerve stump at the time of surgical removal of the eyeball, regardless of the pathological report, is considered a logical procedure.

Some cases of bilateral retinoblastoma may be cured, with a degree of preservation of vision, by radiation therapy of the remaining eye. The authors' experience has been largely with radium therapy. They believe that the treatment of the remaining eye with x-ray therapy, as advocated, is more satisfactory than the use of interstitial irradiation as used in some of their earlier cases.

It seems possible, in view of the demonstrable sensitivity of retinoblastoma to large doses of irradiation, that an early tumor may be treated and cured by irradiation alone. H. HARTUNG, M.D.

MISCELLANEOUS

Sandler, B.: A Preliminary Note on the Planning of Combined Radiotherapy of Carcinoma of the Uterine Cervix. *Brit. J. Radiol.*, 1943, 16: 331.

The need of a combined radium and external-radiation therapy technique has long been acknowledged. This technique should be individualized according to the needs of the patient.

Most radium charts, while good theoretically, are not practical enough, inasmuch as they fail to consider extraneous factors such as: (1) intrauterine tumors affecting the placement of the radium; (2) position of the uterus; (3) tumor invasion of the vaginal fornices and resultant influence on the positioning of the radium; and (4) bulky cervical tumors. The author is endeavoring to correct these discrepancies by the use of a wax mold which outlines the radium applicators as they would appear in the patient. The depth dose can then be calculated.

The importance of external irradiation as an adjunct to radium therapy is stressed. Many therapists, realizing that the lethal radium dose does not reach the lateral pelvic wall, depend on external irradiation to kill cancer cells in this area. In the author's opinion, most routine methods used today are insufficient. In the two-field technique with the center area separated by a lead strip, there may be either an overdose or an underdose between the radium and the external radiation fields. This area is called the "paralethal zone."

For the proper planning of external radiation therapy, a wax model of a pelvis is used. Tomograph films depicting the tumor and true pelvis are taken. The plan is to give a maximum dose to the pelvic wall, to allow a sharp drop in the external radiation where the radium dosage is adequate, and give an adequate dose throughout the entire pelvis. Three basic fields are used (2 posterior fields at 90 degrees to each other with cross field areas directly opposed to the anterior field). In large patients, a fourth circular sciatic field is used with its axial rays at 45 degrees to the other three fields.

A flat hard table with measuring devices is used so that the position and angles of the x-ray beam will always be the same. Opaque media are placed in the vagina and x-rays of the pelvis are taken in the supine and prone positions. By means of a "clinometer" the exact degree of tube tilt can always be duplicated.

The author believes that the foregoing procedure is but a step in the practical solution of accurate radiotherapy in the pelvis. It is not feasible for use as a routine procedure. MAURICE D. SACHS, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Bassett, S. H., Woods, R. R., Shull, F. W., and Madden, S. C.: Parenterally Administered Amino Acids as a Source of Protein in Man. *N. England J. M.*, 1944, 230: 106.

A report is given of a patient who had developed a gastrojejunocolic fistula twenty-three years after gastroenterostomy and for which he was finally treated by subtotal gastric resection, after colostomy had failed to give sufficient relief.

The extremely poor condition of the patient was such as to require special metabolic care. The preoperative and postoperative treatment was devoted to the restoration of normal nitrogen equilibrium. Careful study was made of every source of nitrogen intake and output. When oral protein feedings were not possible, nitrogen replenishment was made by the intravenous or subcutaneous injection of amino acids. The requirements were met by two or three daily injections; usually 50 gm. of amino acids were given intravenously in sixty minutes; this was tolerated with ease by the patient. There were no postinfusion reactions and the lower *p*H of the amino acid solution did not affect the blood.

During several phases of the preoperative and postoperative periods, nitrogen equilibrium was almost completely attained by the amino-acid injections, which served as the sole source of nitrogen. However, despite the clinical manifestations of improvement, the plasma protein level failed to rise more than 0.6 gm. above the initial low level.

The authors observed in the urine of this patient an undetermined nitrogen other than that of urea and ammonia, but probably due to the mode of administration. It appeared that the ideal mixture of of amino acids for man may not yet have been realized. BENJAMIN G. P. SHAFIROFF, M.D.

Streltsov, V. V.: Digestion and Metabolism in High-Altitude Flights. *Am. Rev. Soviet Med.*, 1943, 1: 130.

Studies of the effects of anoxia on metabolism and gastrointestinal function were carried out on experimental animals in the altitude chamber, and similar observations were made on fliers and mountain climbers.

Two phases of the action of anoxia on salivary secretion were observed. In the first stage of ascent with slight degrees of anoxia some increase in salivary secretion occurs; with further ascent this is followed by suppression of the secretion. Disturbances of the salivary secretion persist for several days after a return to sea level. Changes in the composition of saliva occur as well as changes in the amount secreted. It appears that these alterations are due to nervous mechanisms.

Gastric motor activity in animals was studied by the balloon method. The cycles of motor activity were completely abolished at high altitudes. If an animal was raised to a high altitude at the beginning of a cycle of motor activity, that cycle proceeded to completion but the following cycle failed to appear. Periodicity was restored by supplying oxygen or by returning the animal to ground level. Roentgenographs with contrast media showed delay in emptying of the stomach with pylorospasm lasting four hours. The interference with motor function of the gut was most pronounced in the upper segments, especially in the stomach, and faded out in the lower intestines. Although the motility of the intestine does not show much change in anoxia, its secretory and excretory functions are markedly disturbed. Severe anoxia inhibits secretion by the glands of both the Pavlov and the Haidenhain pouches, but with less severe anoxia such inhibition is observed only in the Pavlov pouch. These changes are the result of nervous regulation primarily. If animals receive oxygen at decreased barometric pressure, gastric secretion is restored. While the secretion of the gastric glands is diminished, which conserves acid for the organism, the pancreatic secretion of sodium bicarbonate is increased. This combats the respiratory alkalosis developing during ascents.

In anoxia a marked disturbance in liver function occurs which alters the quantity and composition of the bile. During the first two to six hours at an altitude of from 6,000 to 8,000 meters there is a persistent decrease in the amount of bile flowing from the gall bladder into the intestine, with an increase in viscosity and organic solids, including bile acids and bilirubin, but with a decrease in cholesterol. It is concluded that anoxia disturbs the function of the liver cells directly and that an intermediate nervous mechanism is of less importance. With repeated exposures to high altitudes, liver function shows an adaptation and the disturbance becomes progressively less. Bile pigments are increased apparently because of the increased destruction of hemoglobin.

The observation that high-altitude tolerance is improved with increased carbohydrate intake was confirmed. From the results of their experiments the authors conclude that both the meal schedule and the composition of the diet are of particular importance to flying personnel. Since emptying of the stomach is prolonged, meals should be arranged before flights so that the stomach will be empty at the time of ascent. The various views with respect to the composition of optimum diets for fliers are discussed.

JOHN L. LINDQUIST, M.D.

Vokhmianin, P. F.: Altitude Sickness in Flyers. *Am. Rev. Soviet Med.*, 1943, 1: 140.

This article is based on a study of the manifestations of altitude sickness in active military combat.

Recovery of function after removal of the cause of altitude sickness depends upon the degree of hypoxemia, and for the most part proceeds quickly, so that symptoms often escape the attention of the doctor. Prophylactic measures consist in checking the flyer's functional capacity and in educating the flyer in the nature of altitude sickness and in rules for preventing it during flight.

Anoxia causes disturbances in the functions of various organs and systems but a number of these symptoms appear early in flight and are apparent to the flyer himself. The central nervous system and cardiovascular system are the first to react to hypoxemia. Individuals with a labile autonomic nervous system are inclined to the collaptoid type of cardiovascular reaction. Those presenting the cerebral reaction are most resistant to anoxia and better able to compensate.

There are several phases of altitude sickness. The first phase is characterized clinically by stimulation of the central nervous system with quickening of attention and of psychological reactions. Sometimes there is little stimulation, and one notes reddening and slight cyanosis. The pulse becomes more rapid and the systolic blood pressure rises. The flyer usually feels fine under these circumstances. The phase of stimulation lasts a few minutes and may be followed by a state of compensation. With increase of anoxia, stimulation is replaced by depression of the psychological functions, or the second phase, which is manifested clinically by drowsiness and yawning. The flyer becomes indifferent to his surroundings and exhibits a general slowing of activity. In autonomically labile subjects the stage of cardiac stimulation is often followed by rapidly developing pallor, sweating, slowing of the pulse, and a fall in the systolic and diastolic blood pressures. Following these symptoms hypoxemic collapse develops. In such subjects altitude sickness may give a different picture, however, and instead of reddening, there may be early pallor, sweating, and bradycardia, succeeded by a state of compensation. In man, as in animals, recovery repeats in reverse order the stages of development of the illness.

Since the physician does not see the aviator at the time of acute development of the illness, and since recovery is rapid, the diagnosis depends upon the history, the previous medical record, the estimation of the adequacy with which the flyer fulfilled his duties, observation of peculiarities of behavior, complaints of headache, weakness, or unusual fatigue during or after flight, and physical examination. Signs of altitude sickness must be differentiated from reflexes of other organs, chiefly autonomic and vestibular disturbances. JOHN L. LINDQUIST, M.D.

Taylor, F. H. L., Levenson, S. M., Davidson, C. S., and Adams, M. A.: Abnormal Nitrogen Metabolism in Patients with Thermal Burns. *N. England J. M.*, 1943, 229: 855.

Certain observations on the disturbances of nitrogen metabolism in severely burned patients admitted to the Boston City Hospital, Boston, Massachusetts, as a result of the Cocoanut Grove disaster revealed that azotemia was a common complication of severe burns and was usually of the reversible type. It occurred early and was relieved when the urine output became normal. In this type of azotemia, the restoration of a normal urine output results in a return of the increased nonprotein-nitrogen level of the blood to normal. Since, however, the kidney can clear urea only at a fairly fixed maximum rate, the azotemia may persist for several days.

An irreversible type of azotemia occurred in severely burned patients with hemoglobinemia and hemoglobinuria and who were excreting an acid urine.

In certain severely burned patients with coincidental hemoglobinemia and hemoglobinuria, there was an abnormality in the partition of both the blood and the urine nitrogen, which was associated with the presence of large amounts of residual or undetermined nitrogen. The percentage of total nitrogen of the urine present as urea was low.

It is of some practical importance that sulfadiazine administered to patients with irreversible azotemia gave satisfactory blood levels of the drug and was apparently well cleared by the kidney. Under no circumstances, however, was the drug administered until a normal diuresis was obtained.

Hypoproteinemia was a common finding. A transitory hypoproteinemia was associated with plasma loss and could be restored by simple dietary means. There appeared to be a definite correlation between the progressive type of hypoproteinemia and the severity of the burn. This hypoproteinemia increased in severity until the anasarca level was reached and massive edema developed. The more progressive type was probably due to the loss of large amounts of nitrogen into the urine because of increased protein catabolism, in addition to large losses of nitrogenous material at the burned surface.

The fall in albumin and the reversal of the albumin-globulin ratio encountered early may be theoretically associated with the preferential loss of albumin from the circulating blood because of the relatively low molecular weight of albumin as compared with that of globulin.

It is a frequent observation that burned patients remaining in a hospital for long periods of time while awaiting skin grafting lose considerable amounts of weight. It was found that severely burned patients rapidly lost large amounts of nitrogen into the urine. Obviously, such losses of nitrogen into the urine may cause a marked protein deprivation.

An attempt was made to meet the demand for protein by increasing the protein intake to from 100 to 125 gm. a day. Even at this level, there was a marked negative nitrogen balance in 9 patients with severe burns. Most of the patients with minor burns of less than 10 per cent of the body surface involved responded to the intake of 125 gm. of protein a day with a return of their plasma protein to normal, but in those patients with a continued marked loss of

nitrogen into the urine this did not occur. Indeed, in some of the severely burned patients, it has been calculated that, on the basis of the loss of nitrogen into the urine alone, 300 gm. of protein a day would have been required to maintain nitrogen equilibrium. In addition to this loss, some patients continued to lose large amounts of nitrogenous material from the burned surface for long periods of time. This insensible loss could not be calculated. The restoration of protein under these combined circumstances was a difficult problem, since the amounts required were considerably greater than those the patients could ingest. STEPHEN A. ZIEMAN, M.D.

Nixon, N., Eckert, J. F., and Holmes, K. B.: The Treatment of Agranulocytosis with Sulfadiazine. *Am. J. M. Sc.*, 1943, 206: 713.

It has been the custom to discontinue the administration of the sulfonamides when a patient develops agranulocytosis. Others discontinue the drug when the patient shows a leucopenia. Some observers believe that a falling white count during treatment with sulfa drugs is only a transient condition. However, agranulocytosis has occurred and sulfanilamide and sulfapyridine have been the most frequent causative agents. Patients who develop agranulocytosis may recover spontaneously or die from the original infection plus the added misfortune of the disappearance of the granular leucocytes. Treatment for agranulocytosis by transfusion, liver extract, and pentose nucleotides has not been satisfactory.

Discontinuance of sulfathiazole or sulfadiazine during agranulocytosis is not indicated especially since it has been shown that these drugs are independently effective even in the presence of leucopenia and agranulocytosis. Successful control of a possible overwhelming infection may thus be attained until such time as the bone marrow depression can be safely relieved by stoppage of the drug or by its spontaneous recovery.

The authors report 3 cases of agranulocytosis which developed during the course of possibly fatal infections. Sulfadiazine was continued, nevertheless, until the infectious process was controlled. Later the bone marrow and the cellular defensive mechanism recovered spontaneously.

BENJAMIN G. P. SHAFIROFF, M.D.

Hueper, W. C., and Ichniowski, C. T.: Toxicopathological Studies on the Dye T-1824. *Arch. Surg.*, 1944, 48: 17.

Evans blue, or dye T-1824, is an azo dye produced by the interaction of o-tolidine with Chicago acid (1-amino-8-naphthol-2, 4-disulfonic acid) and has a molecular weight of 960 (Gregersen and Rawson). It has been used for a number of years by numerous workers for the determination of total plasma volume in man and experimental animals and has been tried in the treatment of experimental cancer. In spite of the relatively extensive administration of this dye, almost nothing is known concerning its toxic properties.

The experiments reported were undertaken for the purpose of providing at least some fundamental data on this aspect.

The experiments indicate that the minimal lethal dose of T-1824 given as a single intravenous dose of a 0.5 per cent solution is 10 cc. per kgm. for dogs and cats. The dose is apparently somewhat higher for rabbits, as only 50 per cent of the rabbits died after the intravenous injection of 10 cc. per kgm., and is evidently still higher for rats, of which 40 per cent died after such a dose. It is characteristic for the action of the dye that, because of its prolonged retention in the various organs, it may cause death after a delay of several weeks or even months.

Death occurring several weeks or months after the introduction of doses not causing acute death (within one or two days) is related to the prolonged retention of appreciable amounts of the dye in the tissues of various organs, particularly the testis, epididymis, adrenal glands, liver, kidneys, periaortic connective tissue, teeth, and cartilage.

The heart, liver, lungs, and testes show the most marked degenerative effect of the dye, while the brain and the kidneys exhibit less severe regressive lesions, the development of which is associated with increased vascular permeability.

The clinical administration of the dye in amounts of 5 cc. of a 0.5 per cent or 1 per cent solution to the individual patient is apparently a safe procedure. However, the occurrence of late fatalities among animals given 1 cc. per kgm. of a 0.5 per cent solution is an indication that caution should be exercised in repeated administration of this dye to human beings so as to avoid possible toxic effects.

JOHN E. KIRKPATRICK, M.D.

DUCTLESS GLANDS

Rawson, R. W., Hertz, S., and Means, J. H.: Thiocyanate Goiter in Man. *Ann. Int. M.*, 1943, 19: 829.

The development of goiter in 2 hypertensive patients treated with thiocyanate is reported. Note is made of a third patient seen in consultation, and several cases from the literature are cited.

This type of goiter can probably be prevented by prophylactic doses of iodine and can be relieved by the administration of thyroid even when the use of thiocyanate for hypertension is continued. Thiocyanate goiter is characterized by hyperplasia of the thyroid, symptoms of hyperthyroidism and a low basal metabolic rate, exophthalmos (observed in 1 case), low blood iodine, decreased urinary excretion of labeled iodine, and increased urinary excretion of thyrotropic hormone in the inactivated form.

The theory is presented that thiocyanate blocks the formation of hormone by the thyroid, and that the resulting decrease in concentration of active thyroid hormone in the blood stimulates the production of an excess of thyrotropic hormone by the anterior pituitary gland. Thyroid hyperplasia results but, due to block, no increase in the output of

physiologically active thyroid hormone is possible. An excess of administered iodine may force the block. The use of thyroid by-passes the block and, by substitution, relieves the situation.

WALTER H. NADLER, M.D

Brunschwig, A., Allen, J. G., Owens, F. M., Jr., and Thornton, T. F.: Alloxan in the Treatment of Insulin-Producing Islet-Cell Carcinoma of the Pancreas. *J. Am. M. Ass.*, 1944, 124: 212.

Alloxan, the ureide of mesoxalic acid, when injected intravenously into rabbits and dogs, causes specific necrosis of the islets of Langerhans and the epithelium of the convoluted tubules of the kidneys. In some dogs transitory or prolonged hyperglycemia occurs with relatively little elevation in the blood nonprotein nitrogen. Alloxan is effective in man but much higher doses are required than in animals.

The rationale for the use of alloxan in the treatment of a patient who had an insulin-producing islet-cell carcinoma of the pancreas was that, although these tumors are radioresistant and consequently not amenable to x-ray therapy, a chemical agent with specific toxic effect on pancreatic islet cells might influence favorably the patient's symptoms.

Temporary symptomatic relief was obtained in a white man of thirty-two years, who had rather typical attacks of hyperinsulinism, and in whom exploratory laparotomy in 1939 had revealed two tumors in the tail of the pancreas, which were found to be islet-cell carcinomas. X-ray therapy had had little effect. The attacks of hyperinsulinism were eliminated for brief periods after each series of intravenous injections of alloxan. Death resulted from a complication at laparotomy in December, 1943, when there was no evidence of residual pancreatic tumor, but metastases were found in the liver. Autopsy revealed no evidence of necrosis comparable to that seen in the islet cells in the pancreas of the dog and rabbit resulting from alloxan.

HAROLD C. OCHSNER, M.D.

Greene, H. J., and Lapp, W. A.: Adrenal-Rest Tumor of the Ovary. *Am. J. Obst.*, 1944, 47: 63.

A case of adrenal-rest tumor of the ovary, occurring in a colored female patient and associated with marked changes of defeminization and masculinization, is presented. Surgical removal of the tumor produced regression of most of the signs and symptoms. The patient, when last heard from (more than three years after operation), was enjoying good health. EDWARD L. CORNELL, M.D.

SURGICAL PATHOLOGY AND DIAGNOSIS

Stout, A. P.: Liposarcoma—the Malignant Tumor of Lipoblasts. *Ann. Surg.*, 1944, 119: 86.

A group of 41 cases of liposarcoma has been studied in connection with 134 previously reported cases. These tumors tend to form very large, bulky masses, with a predilection for the thigh and extraperitoneal tissues, but with an occasional appearance in many other regions as well. They exhibit great variations in growth speed, they are sometimes multiple, and the more malignant forms metastasize usually to either the lungs or the liver.

Grossly, these tumors are frequently mottled with yellow, because of their lipoid content, and they are often slimy from the formation of mucoid material. Microscopically, they can be divided into one well differentiated, less malignant group, which simulates the appearance of ordinary embryonal fat, and three other poorly differentiated, more malignant groups, resembling, respectively, atypical ordinary embryonal fat, atypical brown fat with the formation of rounded lipoblasts, and, finally, both of these elements in combination. Probably as a result of metaplasia, these tumors can, on occasion, form other tissues, such as reticulin and bone. This versatility suggests that there are probably no separate embryonal stem cells for adipose tissue and brown fat, but that both spring from a common ancestor segregated from the primitive mesenchyme.

SAMUEL KAHN, M.D.

EXPERIMENTAL SURGERY

Reid, M. R., and Ransohoff, J.: Intravascular Parathyroid Grafts. *Am. J. M. Sc.*, 1943, 206: 731.

In a study of the possibility of transplanting parathyroid grafts, it was believed that the bed should be of loose structure, since tissue pressure would compress the graft. The authors believed it should be vascular, but not sufficiently so to cause the formation of strangulating hematomas. It was decided that the vascular tissue of the lung would meet the requirements and in two series of experiments, parathyroid tissue was removed from its normal site, placed in the external jugular vein and flushed toward the heart with normal saline solution. In the one series homografts were used, and in the second series grafts from other dogs were used.

The dogs surviving the experiments in which homografts were employed showed a progressive decrease in the amount of parathormone and calcium required to keep them clinically free from tetanus. However, 8 of the 11 dogs died, apparently of a tetanic seizure during the night or when they were not observed. Three were sacrificed at five, six, and seven months, respectively. These 3 dogs were apparently free of symptoms at that time.

On the other hand, those dogs which received cross-grafts, got along for a period of from three to five weeks with decreasing amounts of specific therapy. Thereafter, they began to require increasing amounts of parathormone and calcium in order to prevent tetany.

All of the dogs had careful post-mortem examinations of the lungs and in only 2 instances evidence of tissue was found that might be interpreted as being emboli of parathyroid implants. In 1 case, that of a cross-grafted dog which died after two weeks, there was found a fibrous tissue plug about the edges of which were cells microscopically resembling parathy-

roid cells. In one of the dogs with the homografts, which was sacrificed after six months, a similar mass of tissue was found which lacked the normal architecture of a parathyroid gland but resembled it in cellular detail.

It was believed that all the dogs with homografts would have survived had nursing care been available to prevent their death during a tetanic seizure. It was also believed that the cross grafts survived for a while and functioned, but that subsequently they died, just as may happen with cross skin grafts. No clinical signs or symptoms of pulmonary embolism were noted in these animals.

JOHN W. EPTON, M.D.

Rabinovitch, J., and Pines, B.: The Effect of Heparin on Experimentally Produced Venous Thrombosis. *Surgery*, 1943, 14: 669.

A brief discussion of the pertinent factors concerning the mechanism of thrombus formation is presented.

The experiments presented by the authors were performed in an attempt to answer two problems: (1) do the injections of heparin prevent the formation of an intravascular clot if administered prior to injury of the vessel wall, and (2) is heparin effective in causing the solution or disappearance of a clot once the latter has been formed.

Rabbits weighing between 2 and 3 kgm. were used. The normal coagulation time, by means of a fine capillary glass tube, was found to average between three and four minutes. The heparin used was in the form of liquaemin solution. One cubic centimeter of the solution contained the equivalent of 10 mgm. of highly purified heparin. In each of the experiments 1 cc. of liquaemin was diluted with 10 cc. of saline solution before it was injected into the ear vein of the rabbit.

When 1 cc. of the heparin solution was injected into the ear vein of the rabbit the clotting time was found to be prolonged for a period of five hours. Ten minutes after the injection of heparin the blood remained fluid for ten hours. The clotting time gradually decreased until it had returned to normal at the end of five hours. From this it would appear that a reinjection of the anticoagulant is necessary at least every four or five hours.

The jugular veins of the rabbit were used. They were exposed by means of an aseptic technique under ether anesthesia. The veins were isolated for a distance of 2 or 3 cm., grasped between the thumb and index finger, and forcibly pulled so as to injure the endothelial lining. They were then partly constricted at the site of injury with a loose ligature placed around it, care being taken not to completely occlude the lumen.

The practice of this procedure was found effective for producing an intravenous clot in each experiment within from twenty-four to forty-eight hours. Microscopic examination of the vein showed it to be occluded by a thrombus composed for the most part of a marginal zone of blood platelets which adhered at one point to the endothelium of the vein. The rest of the clot was made up of a fine network of fibrin enmeshing numerous red blood cells and scattered leucocytes.

In six experiments in which 1 cc. of liquaemin diluted in 10 cc. of saline solution was injected just before the vein was traumatized, 2 of the rabbits showed a thrombus four days postoperatively. In the 4 other rabbits there was no gross or microscopic evidence of local thrombosis. The injured endothelium had regenerated and there was no break in the continuity of the lumen. Of 6 rabbits to which the anticoagulant was given both preoperatively and postoperatively, none of the animals showed evidence of local clot formation either grossly or microscopically after from two to five days. In these animals heparin was given twice daily for the duration of the experiment.

From these observations it was concluded that the administration of liquaemin both before and after injury to the vessel wall keeps the circulating blood fluid and prevents the formation of a local clot. At the end of four or five days the injured endothelium regenerates completely and thrombus formation does not follow. In the majority of instances a single injection of liquaemin was sufficient to prevent clot formation. In another group of experiments the vein was traumatized and a clot allowed to form in both jugular veins. On the second postoperative day the neck was reopened and one of the veins removed for microscopic study and to serve as control. The animals were then injected with liquaemin twice daily for a period of five or six days. Examination at this time showed that the thrombosis had completely disappeared in 4 of the 5 animals observed and in the remaining animal the vein was partly occluded by a retracting clot. The endothelium of the vessels had regenerated and the continuity of the lumen was re-established. In 2 other series of experiments the anticoagulant was not given until the third and sixth postoperative days, respectively. In the series in which the liquaemin was given on the third postoperative day, 50 per cent of the animals showed a complete disappearance of the clot, while in the series in which the heparin was not given until the sixth postoperative day all of the animals showed occlusion of the veins by an adherent thrombus. In both of these experiments the anticoagulant was given twice daily for eight days.

From these experiments the authors concluded that under certain conditions liquaemin is effective in causing the solution or disappearance of a clot, especially when administered during the very early stages of its formation. It is of no effect when given during the later stages of clot formation, when it is undergoing organization. A few in-vitro experiments were carried out to see if heparin would cause solution of fibrin. No effect was observed. No explanation as to why heparin causes a disappearance of the clot in the early stages is given.

DWIGHT E. CLARK, M.D.

Sellers, E. A., and Willard, J. W.: Effect of Plaster Bandages and Local Cooling on Hemoconcentration and the Mortality Rate in Burns. *Canad. M. Ass. J.*, 1943, 49: 461.

Using anesthetized dogs as experimental animals, the authors studied the effects of the application of plaster bandages and of local cooling in the treatment of experimental burns. After preliminary experiments, an arbitrary standard of burning was selected, according to the weight of the animal.

After anesthetization, the dog's legs were immersed in water for one minute. Hemoconcentration was followed by hourly hemoglobin and hematocrit readings.

In the treated groups, rapid drying, commercial plaster-of-Paris bandages were applied over the burned areas immediately after burning. Care was taken to avoid any initial compression by the bandages. Three groups of experiments were carried out. In the first an 8 per cent burn was produced in the hind limbs of 20 treated and 20 control animals. In the second, an 8 per cent burn was spread over the four limbs of 8 treated and 8 control animals. In the last group, a 15 per cent burn was produced on the four limbs of 6 treated and 10 control dogs. This last burn represented the maximum it was possible to give on the extremities alone. An attempt was made to carry the plastering well above the burn, but this was difficult in the first and third groups, because of the extent of the burn.

For the suspension and cooling experiment a 15 per cent burn was produced on the four legs of 4 dogs. Moistened gauze was loosely applied to the extremities. The limbs were then suspended and a current of air directed over them.

With a similar burn, on 11 control and 12 experimental animals, double-walled rubber sleeves were applied to the four limbs, and water at 8° C. was circulated through the sleeving. The cooling experiments were continued for forty-eight hours.

Very little hemoconcentration occurred in the animals treated by the immediate application of plaster. Where the plastering was carried well above the burn the hemoconcentration was negligible.

The treated dogs showed no evidence of pain or discomfort after the effect of the anesthetic had passed off.

Bloody diarrhea and hematuria were observed in both plastered and control animals for from four to five hours after burning. These signs were frequent and often severe in the untreated animals, less so in the group with plaster. In both groups hemolysis in the blood samples appeared within an hour of the burn. As time passed this increased in severity.

If casts were removed after twenty-four hours the legs appeared normal but soon blistering between the toes and swelling occurred in a similar manner to that in the controls. If the casts were removed after forty-eight hours some swelling occurred but it never became prominent. After seventy-two hours swelling was minimal. When the casts were removed after a longer period (up to eleven days) no swelling was observed, although the deep circulation was well maintained.

At autopsy, marked swelling with blistering between the toes was invariably seen in the control animals. The skin of the legs had a leathery appearance, and a large amount of reddish subcutaneous fluid was present. When the plaster was removed after death, swelling and blistering as well as subcutaneous collections of fluid were absent.

The viscera were usually congested. The lungs, liver, kidneys, adrenal glands, pancreas, and intestines showed this in varying degrees. While congestion occurred in the dogs with plastered extremities, it was less consistent and less severe than in the controls.

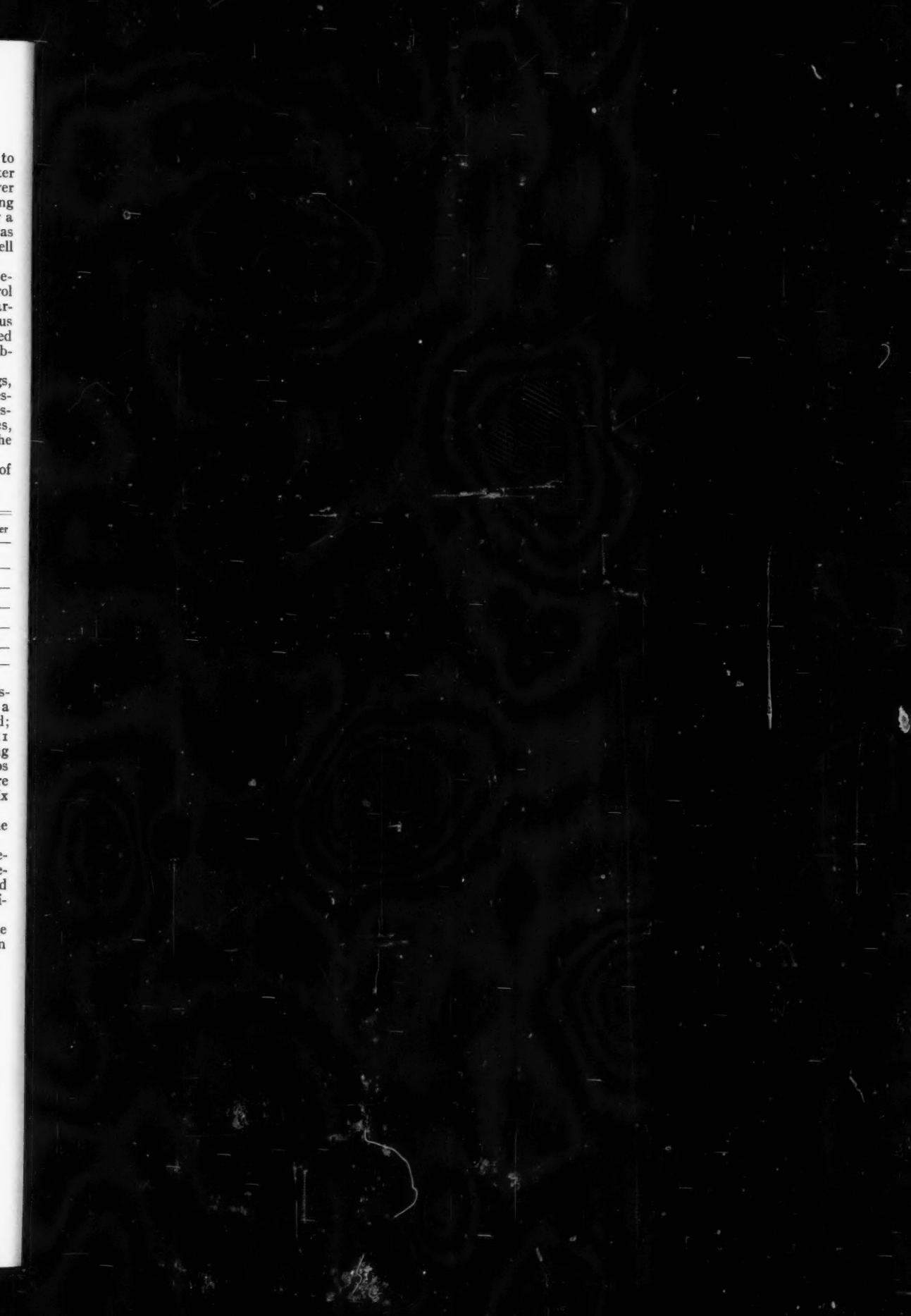
The comparative mortality in the 3 groups of experiments was as follows:

Amount of Burn	Control Animals		Animals with Plaster	
	Died	Lived	Died	Lived
8% (two legs)	11	9	2	18
8% (four legs)	3	5	0	10
15% (four legs)	6	4	0	6
Totals	20	18	2	34
Percentage	52.6	47.4	5.5	94.5

When cooling was combined with minimal pressure, as in the rubber-sleeve experiment described, a drop in the skin temperature of 15° C. was produced; 9 of the 12 treated animals survived and 4 of the 11 controls lived. When cooling was effected by passing a current of air over the moistened suspended limbs of the animal, 3 of 4 dogs died. The skin temperature was kept 10° C. below the normal for a period of six hours in this experiment.

Hemoconcentration was invariably lower in the treated dogs than in the controls.

Pathological findings were similar to those described in the experiments using plaster casts. Hemolysis in blood samples, hematuria, melena, and visceral congestion all occurred, but were more variable and less severe in the treated group.

Pathological findings indicate that even in the absence of hemoconcentration, factors other than fluid loss are of importance in burns.

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